Archives of Neurology and Psychiatry

VOLUME 41 MARCH 1939 NUMBER 3

COPYRIGHT, 1939, BY THE AMERICAN MEDICAL ASSOCIATION

GLIOMAS OF THE PONS

CLINICAL AND PATHOLOGIC CHARACTERISTICS

BERNARD J. ALPERS, M.D.

AND

J. C. YASKIN, M.D.

PHILADELPHIA

Gliomas of the pons present an intriguing problem in diagnosis. They are readily confused with other processes, but if once suspected their diagnosis is in most cases not only possible but easy. Furthermore, their diffusely infiltrating nature gives rise to greatly varied clinical manifestations. It is primarily to define and clarify the clinical features of pontile gliomas, in order to indicate how the diagnosis is made, that 11 cases are recorded in this paper. Incidentally, mention will be made of bizarre clinical features arising from the method of growth of these tumors.

Among all verified gliomas observed between 1929 and 1936 in the neurosurgical clinic of the University Hospital there were 15 infiltrating tumors of the pons. Only 11 of these were selected for study, since 4 have already been described as mesencephalic gliomas (Alpers and Watts [1]). These 4 tumors involved primarily the mesencephalon and secondarily the pons. The 11 tumors described in this paper were primarily pontile, judging by the development of the symptoms and signs.

REPORT OF CASES

CASE 1.—*Diplopia and internal strabismus, followed later by left hemiplegia and cerebellar symptoms. Evidences of paralysis of the oculomotor and both abducens nerves, peripheral paralysis of the left facial nerve; bilateral pyramidal tract signs; cerebellar involvement.*

History.—C. C., a boy aged 8 years, under the care of Dr. F. H. Leavitt in the Graduate Hospital, had had a sore throat twelve weeks before his admission. This was followed immediately by diplopia, which was succeeded three weeks later by an internal squint. Almost at the same time signs of increased intracranial pressure developed, characterized by frontal headaches and projectile

From the Neurosurgical Clinic and Laboratory, the Hospital of the University of Pennsylvania, and the University of Pensylvania Graduate School of Medicine.

1. Alpers, B. J., and Watts, J. C.: Mesencephalic Gliomas, Arch. Neurol. & Psychiat. **34**:1250 (Dec.) 1935.

vomiting. About one month before he entered the hospital he was unable to walk and found that he had a tendency to swing to the right.

Examination.—There were diplopia, with preservation of all ocular movements, and peripheral facial paralysis on the left side, not marked enough, however, to be definite. The only evidences of disease of the pyramidal tracts at this time were a bilateral Babinski sign and hyperactive patellar and weak abdominal reflexes. Cerebellar symptoms were outstanding, with incoordination of both arms and legs, a tendency to fall to the right, past pointing with the left hand and truncal dyssynergia. A diagnosis of encephalitis was made, largely from the history and the involvement of cranial nerves.

Course.—A month later there were, in addition, internal strabismus of the right eye, nystagmus on lateral gaze, left ankle clonus and more definite evidence of peripheral paralysis of the left facial nerve. When the patient was studied in the Graduate Hospital a month later, there were, in addition, partial ptosis of both eyelids, partial internal ophthalmoplegia of the left iris, which was widely dilated, bilateral paralysis of the external rectus muscle, spastic paralysis of the left side and partial spastic paralysis of the right. There was no papilledema, and the spinal fluid pressure was 160 mm. of water. Roentgen examination of the skull showed some separation of the sutures.

During the clinical course of two months, bilateral paralysis of the abducens nerve, signs of involvement of the pyramidal tracts and peripheral facial paralysis had developed. A diagnosis of an expanding lesion in the pons was made, and a ventriculogram, taken by Dr. F. C. Grant, showed dilatation of the lateral and third ventricles, with no visualization of the fourth ventricle.

Gross Examination of the Brain.—Necropsy, which was performed several days later, showed a large pontile glioma, involving both the basis and the tegmentum pontis and extending into the medulla, particularly on the right side. The right pyramid was especially involved (fig. 1). Despite invasion of the basis pontis by the tumor, many fiber bundles could still be seen coursing through it. The pons was enlarged to about twice the normal size. The tumor did not extend into the mesencephalon. The tumor was a glioblastoma multiforme.

Histologic Studies.—Examination of the brain stem explained some of the clinical manifestations, but not others. No evidence of degeneration was observed in the oculomotor nerve or its nucleus on either side, so that the partial ptosis observed clinically was not explained. The nuclei of both abducens nerves and the nerves themselves were degenerated. The facial nerves and nuclei were interesting. The nuclei were degenerated; both nerves were thinned and pushed against the ventricular floor; the course of the nerves through the pons was much distorted. There was definite degeneration of some fasciculi in the left facial nerve at its point of emergence on one side; this was less definite on the opposite side. The trigeminal and auditory nerves were well preserved. The fibers of the medial fillet were thinned. The tumor invaded the basis pontis extensively, but it was surprising how many of the fibers in this region remained intact. In the medulla the tumor produced marked degeneration of one pyramid and less marked loss of myelin sheaths in the other; the involvement was definitely greater on one side; clinically there were spastic hemiplegia on one side and paresis on the other.

Comment.—In this case a large pontile glioma occurred in a boy aged 8. The clinical course was of six months' duration. The onset was confusing because of the history of an infection preceding the diplopia, which was the first symptom noted. This, with fever and a history of an

old sinal infection, focused attention on the inflammatory aspects of the condition and was in part responsible for justifiable early diagnosis of encephalitis.

The onset of the illness with double vision was important, and the relatively early appearance of peripheral facial paralysis was also of great diagnostic import. Particularly interesting was the development, while the patient was under observation, of bilateral paralysis of the

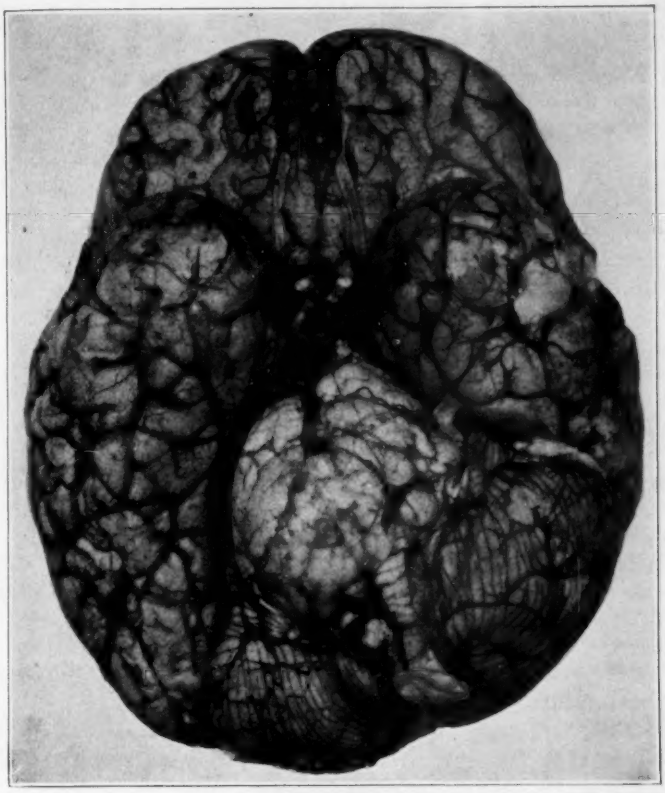


Fig. 1.—Large infiltrating tumor of the pons, extending into the medulla. The pontile enlargement is clearly evident. Note the torsion of the entire brain stem and the deep groove of the basilar artery.

external rectus muscle and the appearance of bilateral signs referable to the pyramidal tracts. The cerebellar signs, which were outspoken during the early phases of the disease, showed relatively little progress during the later stages. One other aspect of this case is important, namely, the absence of objective evidences of increased intracranial pressure at any time. The ocular fundi and the spinal fluid showed no signs of increased pressure.

CASE 2.—*Torticollis, squint and staggering for six months; weakness of the abducens and facial nerves on the left; right hemiparesis; cerebellar signs, chiefly on the right; moderately choked disks; extensive glioma of the pons.*

History.—B. P., a girl aged 7½ years, was noticed five months before her admission to the hospital to be holding her head on one side, chiefly upward and to the right. At the same time headaches appeared in the frontal and temporal areas on the left. For three months she had been troubled by internal strabismus on the left, and for four weeks she had staggered and had difficulty in using the right hand. She had had double vision for some time.

Examination.—There were diplopia, with paralysis of the left external rectus muscle, and papilledema of 2.5 D. in one eye and 3 D. in the other. There was peripheral paralysis of the left facial nerve, the forehead being particularly affected. The right leg and arm, particularly the arm and hand, were weak. The Babinski sign was present on the right. The patellar and achilles reflexes were decreased. There were rather striking cerebellar signs. The child stood with a wide base and showed dyssynergia, especially of the right arm. Romberg's sign was present. Horizontal nystagmus was present bilaterally. The signs remained unchanged during the patient's stay in the hospital. Roentgenographic studies of the skull showed marked convolutional atrophy and widening of the sutures. A diagnosis of pontile glioma was made, and since the tumor was in an inaccessible position no attempt was made to remove it.

Gross Examination of the Brain.—Necropsy revealed a large infiltrating tumor of the pons, extending into the rostral end of the medulla. On the left side of the pons a hemorrhagic mass protruded externally. The tumor compressed the facial and auditory nerves on the left, but the trigeminal nerve escaped. The left inferior olive and the left pyramid were involved by the tumor. Section of the pons showed invasion of the fibers of the pyramidal tract and of the medial lemniscus on the left side. The region of the nucleus of the facial nerve was invaded by tumor, and so, too, were the superior olive and the medial lemniscus at this level. Grossly the nuclei of the abducens nerves did not seem to be involved. Gross sections of the medulla showed definite invasion of both inferior olives, of the left inferior cerebellar peduncle and of the reticular formation. Both pyramids were invaded by tumor. Internal hydrocephalus was present, with enlargement of the entire ventricular system about the fourth ventricle.

Histologic Studies.—The tumor was an astrocytoma. Weigert preparations showed a large glioma which invaded the pons much more on one side than on the other. It destroyed many of the pyramidal and cerebellar fibers in the basis pontis, but left many intact. The entire pontile structure was distorted. On the side of greater involvement the mesial fillet was much smaller than that on the opposite side. Here, too, the formatio reticularis was invaded by tumor. The facial and the abducens nerves and their nuclei were "caught" in tumor on this side. There was invasion of both the basis and the tegmentum on the less involved side as well. In the medulla the tumor was confined almost entirely to one side. Here the pyramid was almost completely destroyed. The other pyramid was normal. On the same side the inferior olive, the inferior cerebellar peduncle and the gray substance in the floor of the medulla were invaded. The vestibular area and the auditory nerve were also involved. Although the vestibular nuclei were invaded by the tumor, the auditory nerve in its intramedullary course was normal in appearance; only in its extramedullary portion was it degenerated. The

posterior longitudinal bundle was much distorted and partially degenerated on this side, as was the mesial fillet. The various tracts in the medulla were invaded by tumor.

In this case, as in the others, there was much more extensive anatomic involvement than the clinical symptoms indicated.

Comment.—In this case, as well as in the case immediately following, torticollis was an early symptom. It was followed shortly by diplopia and internal strabismus, which were succeeded by symptoms of cerebellar involvement and signs referable to the pyramidal tracts. Palsies of the cranial nerves, paralysis of the left abducens (sixth cranial) and the left facial (seventh cranial) nerve, disease of the pyramidal tracts and cerebellar signs completed the picture. Unlike the findings in case 1, there was a moderate degree of papilledema, with subjective complaints of increased intracranial pressure. The internal squint and diplopia were among the earliest and most persistent symptoms; indeed, the patient found it necessary to wear a cover over the left eye to correct the diplopia. Extensive as the tumor was, it produced only a relatively low degree of papilledema and moderately increased pressure.

CASE 3.—*Diplopia; tilting of the head; incoordination; paralysis of the abducens and the facial nerve on the right; bilateral pyramidal signs, more pronounced on the right; paralysis of the motor portion of the left trigeminal nerve; loss of the pharyngeal reflex on the left; bilateral reduction in hearing; cerebellar signs; homonymous right upper quadrantanopia.*

History.—C. H., a girl aged 10 years, in the service of Dr. W. G. Spiller, had double vision for about two months before her admission to the hospital. It was noted at the same time that her head was tilted to the right. For a month she had been awkward in her movements; this condition was followed by dizziness, trouble with walking and incoordination in all four extremities.

Examination.—The abducens and the facial nerve on the right were paralyzed. In addition, there was paralysis of the muscles of mastication on the left, without involvement of the sensory portion of the trigeminal nerve except for decreased conjunctival sensation. The pharyngeal reflex was absent on the left but present on the right. There was slight deviation of the tongue to the right. The right arm and leg were weak and the left less so, and there were a bilateral Babinski sign and ankle clonus. Sense of position was lost in the right hand. Astereognosis was present on the left side. There were both horizontal and vertical nystagmus and ataxia and dyssynergia of the left arm. The tendon reflexes were uneven; they were definitely increased in the right arm and leg, and the left patellar reflex was hyperactive. Dyssynergia was present on both sides but was more marked on the right. There was no evidence of papilledema. The spinal fluid pressure was 130 mm. of water. There was a right homonymous upper quadrantanopia. Suboccipital craniectomy was performed and was followed by death in two days.

Gross Examination of the Brain.—Necropsy revealed a large infiltrating tumor filling the entire pons and extending posteriorly into the medulla and anteriorly into the posterior portion of the midbrain (fig. 2). Externally the left trigeminal nerve appeared flattened, the motor root especially being much smaller than normal. The left abducens nerve was compressed by tumor. The pons was about

twice the normal size, the tumor invading the basis pontis in its entirety, but more extensively on the left. The tegmentum pontis was compressed, and the left middle cerebellar peduncle was invaded by tumors. As the tumor extended posteriorly it entered the medulla, where it appeared as a nodule about 1 cm. in diameter, involving the olive and pyramid on the left side. Anteriorly the tumor invaded the midbrain, involving the lower portion, notably the red nucleus, the substantia nigra and the pes pedunculi.

Histologic Studies.—The tumor was an astrocytoma. Careful study of the brain stem both by the Weigert stain and by cell stains revealed interesting changes. In the mesencephalon there was almost complete destruction of the brain tissue on the right, except for a small portion around the iter. On the left

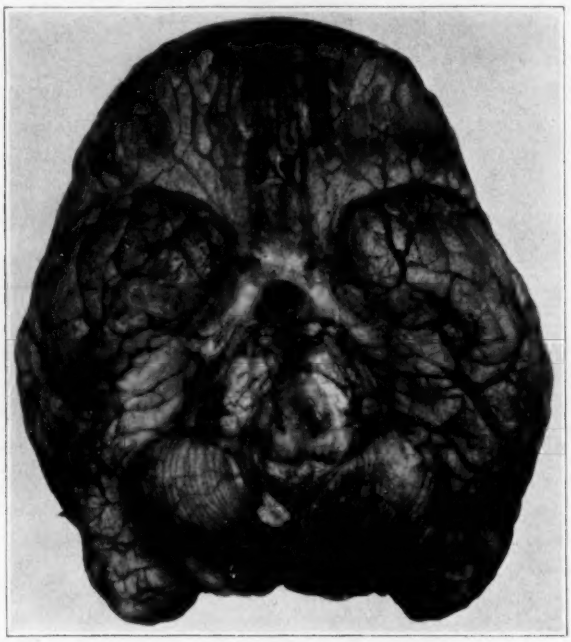


Fig. 2 (case 3).—Large pontile tumor extending into the medulla. Note the extension into the left side of the medulla, where the tumor is seen as a large nodule.

side a much larger portion of tissue remained intact. On this side the lateral geniculate body was invaded by tumor. In the pons the right abducens nucleus was decreased in size, and its cells were degenerated; on the left this nucleus was completely destroyed. The basis pontis was invaded by tumor, but numerous fibers were still intact. Careful study of the trigeminal area on both sides revealed nothing conclusive in trigeminal nuclei except that on one side the motor nucleus seemed more degenerated than on the other. On one side of the pons, furthermore, the locus caeruleus was definitely degenerated as compared with that on the other. Weigert sections showed definite thinning of the mesencephalic root of the trigeminal nerve on one side. On one side the fibers of the mesencephalic root were almost all absent, while on the other, though not all

present, they were observed in considerable numbers. In the medulla there was destruction of one pyramid and the lower portion of the inferior olive. On this side the entire medulla was enlarged. Oddly, the acoustic nerve of the opposite (right) side was degenerated, while that on the side of the tumor appeared intact.

Comment.—Diplopia initiated the clinical picture in this case and was accompanied by torticollis. As in the preceding cases, double vision was one of the first symptoms noted, if not the first. There were palsies of the cranial nerves, as in the preceding cases, but in addition to paralysis of the abducens (sixth) and the facial (seventh) nerve, which characterized the preceding cases, there were involvement of the motor trigeminal (fifth) nerve on the left, absence of pharyngeal sensation on the same side, referable to the tenth nerve, and bilateral reduction in hearing, referable to the eighth nerve.

The nucleus ambiguus on the left side was almost totally destroyed, whereas the dorsal nuclei and the right nucleus ambiguus of the vagus nerve were intact. This probably explains the loss of pharyngeal function on the left.

The right homonymous quadrantanopia was certainly not part of a pontile syndrome. Weigert preparations showed extensive involvement of the left lateral geniculate body, and I am inclined to explain the defect of the visual fields on this basis. No other portion of the visual pathway was involved.

In this case, too, there was no increase in pressure as seen in the fundi or the spinal fluid pressure, despite the fact that the tumor was extremely extensive. The increased complexity of the clinical picture in this case is explained satisfactorily by the fact that the tumor had spread from the pons upward into the lower portion of the mesencephalon and downward into the medulla, where it involved some of the nuclei of the left side, causing loss of pharyngeal sensation on the left and slight deviation of the tongue to the right.

CASE 4.—*Internal strabismus on the right; facial weakness on the right; cerebellar signs; dysphagia; involvement of the trigeminal and the hypoglossal nerve on the right; minor pyramidal signs. Extensive glioma of the pons.*

History.—S. M., a boy aged 7 years, was well until August 1934, when he had intermittent attacks of excruciating epigastric pain. A few weeks after this he was struck on the head by a small stone, but suffered no ill consequences. A week later he began to have daily attacks of projectile vomiting. Within a few days his mother noticed an internal squint of the right eye, and the patient complained of diplopia. A few days later there were facial weakness on the right and severe cerebellar disturbances, so that he was soon unable to walk without assistance. There then developed twitching of the extremities, difficulty in swallowing, gradual reduction of mental processes and, finally, difficulty in starting the flow of urine.

Examination.—There were unequal pupils, the left being larger than the right, loss of vision, especially in the right eye, and paralysis of the right external rectus

muscle. The corneal reflex was absent on the right; the jaw deviated to the right, and there was loss of sensibility to pain and light touch over the first and second divisions of the right trigeminal nerve. There were peripheral paralysis of the right facial nerve, deafness in the right ear, weakness of the right side of the palate and deviation of the tongue to the right. Dyssynergia was present, involving both the upper and the lower limbs, and a Babinski sign was observed on the right. There was no sign of increased pressure on roentgen examination. There was blurring of the nasal margin of the right optic disk, but not of the left.

Gross Examination of the Brain.—The pons was large and was infiltrated by tumor. Involved in the tumor mass were the trigeminal, abducens, facial and auditory nerves on the right. The tumor extended into the mesencephalon and medulla. It was a glioblastoma multiforme.

Comment.—This case is of interest because of the rapid development of symptoms during three months, beginning with vomiting and followed by signs referable to the cranial nerves, especially paralysis of the right abducens and facial nerves. These were followed by other cranial nerve signs and by severe cerebellar disturbances. In this case there were especially well marked signs of lesions in the cranial nerves (the fifth, sixth, seventh, tenth and twelfth nerves on the right) and cerebellar disturbances; involvement of the pyramidal tract was shown only by the Babinski sign on the right. Involvement of the cranial nerves was exclusively unilateral.

CASE 5.—*Partial paralysis of both oculomotor nerves; bilateral paralysis of the abducens and facial nerves; hemiparesis on the left; dyssynergia of the right arm. Extensive glioma of the pons.*

Examination.—I. B., a girl aged 4 years, was admitted on March 6, 1936, to the service of Dr. C. H. Frazier. The only available history was that she had had headache, vomiting and weakness of the left arm and leg for four and one-half months. Neurologic examination revealed inequality of the pupils, the left being larger than the right, bilateral paralysis of the internal rectus muscle, complete paralysis of both external rectus muscles, complete peripheral facial paralysis on the right and almost complete peripheral facial paralysis on the left, except for retention of ability to close the left eye feebly. The left arm was almost completely paralyzed; the left leg was weak. There was severe ataxia of the right arm. There was no papilledema and no roentgenographic evidence of increased intracranial pressure.

Gross Examination of the Brain.—The pons was greatly enlarged, especially on the right. The right side of the medulla was enlarged. The right oculomotor nerve was compressed by tumor; the left was normal. The right trigeminal nerve was firmly embedded in tumor. Both abducens nerves were thin and compressed. The tumor invaded the base of the pons chiefly, more on the right side than on the left. It extended back into the cerebellum, chiefly into the vermis, and also into the medulla. The tumor was a glioblastoma multiforme.

Comment.—This case illustrates the characteristic combination of signs of involvement of the cranial nerves, pyramidal tract and cerebellar pathways by extensive pontile gliomas. The cranial nerve signs, which

were the most striking feature of the case, included partial involvement of the oculomotor (third) nerve bilaterally, complete paralysis of both abducens (sixth) nerves and bilateral paralysis of the facial (seventh) nerve. Despite the absence of increased intracranial pressure, the diagnosis was not difficult, especially in the presence of bilateral paralysis of the external rectus muscles and peripheral facial paralyses combined with pyramidal and cerebellar signs.

CASE 6.—*Facial paralysis; paralysis of the right external rectus muscle; decreased hearing on the right; weakness of the right side of the palate; vomiting and headache; difficulty in walking and swallowing. Glioma invading the pons and medulla.*

History.—H. W., a boy aged 11, was admitted on Nov. 21, 1933, to the service of Dr. C. H. Frazier. Five months previously there developed an internal squint, with diplopia and failing vision. Two months later headaches and vomiting appeared. A month after this the boy noticed difficulty in walking, with a tendency to stagger to the right. There followed, in the last month of the illness, coughing, difficulty in swallowing and weakness of the right side of the face.

Examination.—There were unequal pupils, the right being larger than the left. The corneal reflex was decreased on the right. There was complete paralysis of the right external rectus muscle, the right eye being held in internal strabismus. There were peripheral paralysis of the right facial nerve, diminished hearing on the right and weakness of the right side of the palate. Cerebellar signs were moderately pronounced; the gait was unsteady, with a definite tendency to reel to the right, and there was dyssynergia of the right leg, noted especially in the heel to knee test. Horizontal nystagmus was present bilaterally. The only evidence of involvement of the pyramidal tracts was a slight weakness of the right leg and an inconstant Babinski sign on the right. Roentgen studies of the skull showed slight convolutional atrophy and slight widening of the sutures; this, however, was not convincing evidence of increased pressure. Examination of the ocular fundi revealed no papilledema. There was loss of hearing of 34 per cent in the right ear. A Bárány examination suggested an atypical lesion of the cerebellopontile angle.

Gross Examination of the Brain.—The pons was only slightly enlarged; its surface had the typical verrucose appearance of an infiltrating pontile tumor. The basis pontis in the anterior portion was only slightly invaded by tumor; in the posterior portion the tumor invaded the right side of the base and tegmentum of the pons. This mass extended posteriorly to invade the medulla particularly, but involved also the left side. The entire right side of the medulla was invaded, except for a small portion just under the floor of the fourth ventricle. There was no sign of internal hydrocephalus. Histologic study revealed that the tumor was an astrocytoma.

Comment.—In this case, also, signs of involvement of the cranial nerves, pyramidal tracts and cerebellar pathways were present. The cranial nerve signs were the most striking feature of the case. Again, they were entirely unilateral; they involved on the right side the abducens (sixth), the facial (seventh) and the vagus (tenth) nerve. Cerebellar signs were moderately marked. The signs referable to the pyramidal

tracts were few and included only weakness of the right leg. Of most importance was the onset with paralysis of the external rectus muscle followed progressively by other signs of involvement of the cranial nerves. This is important evidence of a pontile glioma.

CASE 7.—*Diplopia; staggering gait; weakness of the legs; paralysis of the left external rectus muscle; weakness of the left side of the face; deafness of the left ear; cerebellar gait; cerebellar signs on the right; hyperreflexia on the left. Glioma invading the basis pontis and the left side of the medulla.*

History.—C. C., a man aged 45, was admitted on March 30, 1937, to the service of Dr. F. C. Grant. Two months previously he had had an attack of grip, which was followed shortly by diplopia and blurred vision. Ten days later there appeared staggering gait and weakness of both legs. This continued until two weeks before his admission to the hospital, when there were difficulty in swallowing, indistinct speech, bilateral tinnitus and increased staggering.

Examination.—The puplis were unequal, the right being larger than the left. Lateral nystagmus was present bilaterally. There were paralysis of the left external rectus muscle and complete peripheral facial paralysis on the left. The left ear was completely deaf. Dyssynergia was present bilaterally, but was more pronounced on the right. The gait was staggering. There was no frank evidence of involvement of the pyramidal tracts, except increased reflexes on the left. There was no papilledema. The visual fields showed right homonymous inferior quadrantanopia. There was no roentgenographic evidence of increased intracranial pressure. Bárány examination pointed to a tumor of the left cerebellopontile angle.

Gross Examination of the Brain.—The pons was soft and fluctuant. A soft hemorrhagic mass was invading both the basis and the tegmentum of the pons. The left side of the medulla was enlarged.

Histologic Studies.—The tumor was a glioblastoma multiforme. Studies of the pons revealed extensive destruction of the nuclei of the abducens and facial nerves on the left, as well as complete destruction of the intramedullary fibers of these nerves. The cochlear portion of the left auditory nerve in the medulla was completely destroyed.

Comment.—This patient had signs referable to the cranial nerves and cerebellar pathways, with only hyperreflexia on the left to indicate involvement of the pyramidal tract. The cranial nerves (the left abducens and the left facial) were involved unilaterally, as in the preceding case. The onset with diplopia and paralysis of the external rectus muscle was important in establishing the diagnosis. The progressive course made the diagnosis possible, despite the confusing history of "grip" before the onset of the illness and the absence of increased intracranial pressure. The deafness was due to invasion of the medulla and complete destruction of the cochlear nerve.

CASE 8.—*Weakness of the internal and external rectus muscles on the left; peripheral facial paralysis on the left; bilateral pyramidal signs, with absence of cerebellar signs. Extensive glioma of the pons, medulla, mesencephalon and cerebellum.*

History.—B. P., a girl aged 2 years and 9 months, was admitted to the service of Dr. C. H. Frazier on Dec. 3, 1935. The history was indefinite. At 9 months of age the patient had had attacks of breath holding, during which she became cyanotic but did not lose consciousness. Later these attacks were attended by fainting, and on one occasion, about a year before admission to the hospital, by loss of consciousness and rigidity of the limbs. About three months before her admission it was noted that the left leg was thrown far forward in walking. About one month prior to admission the legs were stiff and speech was unintelligible.

Examination.—There was spasticity of the limbs and trunk. The spine was arched, and the neck and spine were curved to the left. The arms were moderately hypertonic and the legs extremely spastic. All the tendon reflexes were hyperactive. There was a Babinski sign bilaterally. Paralysis of the internal and external rectus muscles was present on the left. The left eye could be moved only up and down. There was peripheral facial paralysis on the left. The tongue deviated to the left. No papilledema was seen, but the spinal fluid pressure was 230 mm. of water. Roentgenographic studies of the skull revealed no signs of increased intracranial pressure.

Gross Examination of the Brain.—There was an extensive infiltrating tumor of the pons, mesencephalon and medulla. The pons was almost completely destroyed by tumor. The entire basis pontis and almost all the tegmentum were destroyed. Only a small portion of the tectum remained. In the mesencephalon the tumor invaded the cerebral peduncles and also the nucleus ruber and substantia nigra of one side. In the medulla the tumor extended under the floor of the fourth ventricle and invaded the reticular formation. The middle cerebellar peduncle was invaded bilaterally, and the tumor extended into the white matter of the cerebellum by means of these peduncles. The tumor was an astrocytoma.

Comment.—This case differs from the others in the presence of severe bilateral involvement of the pyramidal tracts, as shown by the marked spasticity of all limbs, especially of the legs. Paralysis of the left oculomotor (third cranial) nerve, and peripheral paralysis of the left facial (seventh cranial) nerve and probably impairment of the vagus (tenth cranial) nerve completed the picture. Despite the extensive nature of the tumor, there was no papilledema, and the spinal fluid pressure was only slightly elevated. Cerebellar signs were not present in this case, but were undoubtedly masked by the spasticity.

CASE 9.—*Involvement of the trigeminal, abducens and facial nerves on the left and of the pyramidal tract on the right; moderate disturbances of sensation on the right, with absence of cerebellar disturbances. Extensive glioma of the pons and mesencephalon.*

History.—A woman aged 20 was admitted to the service of Dr. C. H. Frazier on Aug. 15, 1933. She had had headaches for two months, followed soon by dizzy spells. After this there developed in rapid succession diplopia, slight difficulty in sleeping and swallowing and definite weakness and numbness of the right arm and leg. Finally, before her admission to the hospital, recurrent nausea and vomiting developed.

Examination.—There were complete paralysis of the left external rectus muscle and paresis of the left superior rectus muscle, resulting in limitation of upward

movement of the left eye. There was bilateral loss of the corneal reflexes. The left masseter and temporal muscles contracted weakly, and the jaw deviated to the left. There were peripheral facial paralysis on the left and deviation of the tongue to the left. There were right hemiparesis with increased reflexes and a Babinski sign on the right. The sensations of touch, pain and temperature were decreased over the left side of the face and over the right arm, leg, hand, foot and trunk. There was slow horizontal and vertical nystagmus. There was no papilledema and no roentgen evidence of increased intracranial pressure. Spinal puncture was not performed.

Gross Examination of the Brain.—The pons was much enlarged by an infiltrating tumor. Both trigeminal nerves were involved in the tumor, especially the left; both these nerves were infiltrated by tumor cells. The left abducens nerve and all the nerves on the left side of the medulla were also involved in the tumor. Both the tegmentum and the basis of the pons were infiltrated, the left side being definitely more affected than the right. The cerebellar peduncles were infiltrated, and the tumor extended into the cerebellum along the peduncles of the pons. The left inferior olive, the pyramid and the reticular substance in the medulla were invaded by tumor. The left side of the mesencephalon was also infiltrated by tumor. There was a moderate degree of internal hydrocephalus. The tumor was an astrocytoma.

Comment.—In this case there was extensive involvement of the cranial nerves—bilateral involvement of the trigeminal (fifth) nerve and involvement of the abducens (sixth), facial (seventh), vagus (tenth) spinal accessory (eleventh) and hypoglossal (twelfth) nerves on the left. In addition, there was involvement of the pyramidal tract on one side, but no cerebellar disturbances, despite the invasion of the cerebellar peduncles and of the cerebellum itself. One feature was particularly striking, namely, the sensory disturbances involving the left side of the face and the right side of the body in a distribution similar to that of occlusion of the posterior inferior cerebellar artery. The sensory findings in themselves are unusual in cases of pontile tumor, but in the distribution in this case they are even more fascinating.

CASE 10.—*Headache, blurred vision and awkwardness of the legs; slight involvement of the trigeminal, abducens and facial nerves on the right; deafness on the right. Glioma of the pons.*

History.—N. S., a man aged 32, was admitted on Jan. 11, 1924, to the service of Dr. C. H. Frazier. He had had headaches and pains in the head for from three to four months. He had noticed that he became giddy on bending over and on straining at stool. He had noticed blurred vision for two months and, more recently, awkwardness in dancing and in the use of the legs in general.

Examination.—There was a decreased corneal reflex on the right, with decreased sensations of touch and pain over the right side of the face and tongue. There was slight weakness of the external rectus muscles. The right side of the face was somewhat flattened when at rest, but there was no actual paralysis. Deafness was complete in the right ear. There were horizontal nystagmus, slight incoordination of the right arm and a Romberg sign. There was no choking of the disks.

At necropsy an extensive tumor of the pons was observed. It extended into the right cerebellar hemisphere.

Comment.—There were relatively few findings in this case. There was a combination of signs referable to the cranial nerves (the fifth, sixth and eighth) on the right and to the cerebellar pathways. The pyramidal tract was not affected. Sensation was disturbed over the right side of the face.

CASE 11.—*Bilateral paralysis of the abducens nerve; faciobrachial monoplegia on the left; bilateral Babinski sign; cerebellar symptoms. Pontile glioma.*

History.—A girl aged 9 years was admitted to the service of Dr. J. C. Yaskin in the Graduate Hospital on Aug. 14, 1937. She was said to have had "some extraocular palsies" in May 1936; these were partially corrected by operation. She remained well until August 1937, when there developed awkwardness in the use of the legs, a tendency to fall to the right and thickness of speech.

Examination.—The pupils were equal and reacted promptly to light. The optic disks were well defined except for some infiltration of the nasal margins. There were complete paralysis of the left external rectus muscle and incomplete paralysis of the right external rectus muscle. The left corner of the mouth was weak on voluntary motion. The left arm was weak, but there was good power in both legs. The gait was unsteady, with a tendency to swing to the right. All the tendon reflexes were hyperactive, and there was a Babinski sign bilaterally. No sensory disturbances were elicited.

The spinal fluid pressure was increased (285 mm. of water). There were 18 lymphocytes per cubic millimeter of spinal fluid, but the Wassermann reaction was negative. Roentgen studies of the skull revealed increased convolutional markings.

Antisyphilitic remedies were of no avail, and the patient died of respiratory failure within a month.

Gross Examination of the Brain.—There was a large pontile tumor. The pons was much enlarged; its surface was verrucose. Both abducens nerves were embedded in tumor. The tumor was an astrocytoma.

Comment.—The diagnosis in this case was difficult. The absence of sensory findings was misleading, and the presence of pleocytosis led to a suspicion that syphilis might be a factor in causing the clinical picture. However, the onset with paralysis of the external rectus muscle, followed by progressive involvement of the pyramidal and the cerebellar pathways, made the diagnosis inevitable despite the absence of increased intracranial pressure.

CLINICAL CHARACTERISTICS OF PONTILE GLIOMAS

Age and Sex.—Most pontile gliomas occur in children. Of the 11 tumors in this series, 8 occurred in children below 11 years of age. The age incidence varied in these 8 cases from 2 years and 9 months to 11 years, the average being 7.3 years. In the other 3 cases the ages were 20, 32 and 45, respectively. Pontile gliomas are, therefore, not exclusively tumors of childhood, but much more frequently encountered in children than in adults. Five of the tumors occurred in males and 6 in females.

Duration of Symptoms.—The duration of the symptoms varied from four and a half weeks to fourteen months. The duration of symptoms in the 11 cases was: four and one-half weeks in 1 case, two months in 3 cases, three months in 4 cases, five months in 2 cases and ten months in 1 case. The average duration was three and three-tenths months. In general, the symptoms were of short duration, a surprising finding in view of the slow growth of many of the tumors. Histologically the appearance of the tumor in many instances was not in keeping with the duration of the symptoms before the patient's admission to the hospital. The tumor must have been growing in the basis pontis for some time before evidence of its presence was found. This was due partly to the fact that certain gliomas may grow without destroying much of the invaded brain tissue and partly to the fact that the pons may expand within the posterior fossa without causing many signs of increased pressure.

Mode of Onset.—The onset of symptoms was not uniform. In most of the cases the illness began with diplopia (5 cases) and headache (4 cases). In 1 case the first symptom was holding the head to one side, and in another this symptom was noted almost simultaneously with the diplopia. In only 1 case was facial paralysis noticed by the patient, despite the fact that on examination the facial nerve was not infrequently observed to be affected. Cerebellar symptoms were prominent (6 cases) early in the course of the disease. They usually developed shortly after the first symptoms appeared and were variously described as inability to walk, staggering and awkwardness of gait. Symptoms referable to the pyramidal tract (3 cases) almost invariably appeared late in the clinical course and were as a rule overshadowed by other symptoms. In 1 case the first symptom was sore throat, which was followed soon by other symptoms of involvement of the brain stem. This symptom is mentioned merely to point out that many a case of pontile glioma is first regarded as one of encephalitis; frequently a misleading history of onset with an infection is obtained. It may be stated definitely that as a rule once the symptoms of pontile glioma appear, the development of the tumor is rapid and progressive. As has already been pointed out, the average duration of symptoms is a little over three months, a short course but not surprisingly so in view of the number of tracts interrupted by the tumor.

Paralyses of Cranial Nerves.—Perhaps the most striking of all the signs of pontile glioma were the paralyses of the cranial nerves, which were present always in greater or lesser degree. The abducens nerve was most frequently affected. It was involved in 9 of our 11 cases, in 2 bilaterally. This is not surprising in view of the location of the abducens nucleus in the pons. The facial nerve was affected almost as frequently;

in 4 cases it was involved on the left, in 3 on the right, and in 1 bilaterally. As a rule the paralysis ensuing from involvement of the facial nerve was complete, typical peripheral facial paralysis. In a few instances it was not complete, some parts of the face being affected more than others. In 2 cases the facial paralysis was progressive, so that in the early stages of the disease it was hard to be sure whether the paralysis was peripheral. In these cases progressive weakness of the muscles supplied by the facial nerve developed while the patient was under observation. The trigeminal nerve was involved in 6 cases; its mode of involvement was not similar in all instances. In 2 cases the only manifestation of involvement of this nerve was decrease or absence of the corneal reflex. In 1 case only the motor portion of the trigeminal nerve was affected; in 2 cases both the motor and the sensory portion were affected, and in another case the sensory portion was affected to the exclusion of the motor portion. This is somewhat similar to the experience of Horrax,[2] who in 11 of his 15 cases of pontile glioma observed disturbances of the trigeminal nerve. Of these, 6 were sensory, 4 motor and 1 both sensory and motor. The dissociation of trigeminal involvement has been observed not infrequently in cases of pontile gliomas. Usually the motor portion is involved and the sensory portion escapes. Sometimes, however, the sensory portion is involved to the exclusion of the motor portion. Motor paralysis without sensory involvement has been noted by Bassoe and Apfelbach,[3] who found paralysis of the left masseter muscle with intact sensation over the left side of the face in a case of pontile glioma. The auditory nerve was affected in only 3 cases; in 2 there was loss and in 1 only slight diminution of hearing. In 3 cases the vagus nerve was affected, this disturbance being always manifested by difficulty in swallowing and palatal weakness. The hypoglossal nerve was involved in 2 instances. In only 4 cases was there involvement of the oculomotor nerves; in 1 the only manifestation was inequality of the pupils, and in the other 3, paralysis of isolated muscles innervated by the oculomotor nerve.

Paralyses of the cranial nerves were usually unilateral. In 8 of the 11 cases the cranial nerves were affected exclusively on one side, and in only 3 was there bilateral involvement. In these 3 cases the cranial nerves were affected in the following manner: the left facial nerve and both abducens nerves in case 1; the right trigeminal nerve motor portion, the right abducens nerve, the right facial nerve, the left vagus nerve (loss of the pharyngeal reflex) and the left trigeminal nerve (loss of the

2. Horrax, G.: Differential Diagnosis of Tumors Primarily Pineal and Primarily Pontile, Arch. Neurol. & Psychiat. **17**:179 (Feb.) 1927.

3. Bassoe, P., and Apfelbach, C. W.: Glioma of the Bulb and Pons, Arch. Neurol. & Psychiat. **14**:396 (Sept.) 1925.

corneal reflex) in case 3, and the oculomotor, the abducens and facial nerves bilaterally in case 5. This predominantly unilateral involvement of the cranial nerves is surprising in view of the diffusely infiltrating character of pontile gliomas and the small area of brain tissue invaded. One would expect to find bilateral involvement of the cranial nerves as a rule, but this presumption is not borne out by the facts.

Pontile gliomas, therefore, produce usually unilateral, but sometimes bilateral, involvement of the abducens, the facial and the trigeminal nerve, in the order named. Sometimes involvement of the auditory, vagus and hypoglossal nerves occurs when the medulla is invaded, and disturbances of the oculomotor nerve are observed when the mesencephalon is involved.

Motor Paralyses.—Motor paralysis or some involvement of the pyramidal tracts was frequent in our cases of pontile glioma. In 10 of the 11 cases reported, some form of involvement of the pyramidal pathways was observed. In 7 cases hemiparesis was present. In 2 cases there was bilateral involvement of the pyramidal tracts, producing incomplete quadriplegia. In 1 case the only sign of involvement of the motor tract was hyperreflexia on one side, and in another only a Babinski response was present. In 1 of the cases in which there was bilateral involvement, only a bilateral Babinski sign was noted at first, but later quadriplegia developed. In 4 of the 7 cases (55 per cent) in which there was frank weakness of one side there was hemiplegia alternans. This frequency is about the same as was observed in Horrax' series, in which 9 of 15 patients (60 per cent) showed this symptom.

It is clear, therefore, that motor paralyses are commonly associated with pontile glioma, but that they are manifested in various ways. The most common manifestation is hemiparesis. The paralysis in such cases is not complete and sometimes does not affect the face. This is true in cases in which the infiltrating tumor lies chiefly below the level of the facial nucleus. The reason for the hemiparesis is clear; the fibers of the pyramidal tract are widely separated in the basis pontis, so that a large lesion would be required to cause their complete interruption. In addition, the nature of the infiltrating tumor in the pons is such that there is not complete destruction of the fibers; many of them pass through the tumor and are still intact. The common occurrence of hemiparesis with a pontile glioma is surprising until one realizes that frequently one side of the pons is more severely invaded than the other. Despite this, the unilateral weakness is difficult to explain because, while one side of the pons is more invaded than the other, postmortem examination usually reveals bilateral invasion, especially of the basis pontis. Bilateral involvement of the pyramidal pathways clinically, however, is not common. In some cases the only manifestation of involvement of the pyramidal tracts

may be a Babinski sign, which may be unilateral or bilateral. This sign in the presence of ocular paralysis and other signs may be of great diagnostic importance.

Cerebellar Signs.—Signs of involvement of the cerebellar pathways were present in 10 of the 11 cases. This was to be expected in view of the fact that pontile gliomas invade the basis pontis chiefly and are therefore certain to interrupt cerebellar pathways from the cortex to the cerebellum. In some instances the tumor extended directly into the cerebellum and produced cerebellar signs in this way.

The clinical expression of cerebellar involvement varied greatly. In only 1 case was there bilateral dyssynergia involving the arms and legs. The distribution of the dyssynergia in the other cases was: right arm and leg (1 case), left arm (1 case), right arm (2 cases), both arms (1 case) and trunk and legs (1 case). This considerable variation was less important in diagnosis than the fact that some sort of cerebellar involvement was present in almost every case. In 1 case the only sign of cerebellar disease was horizontal and vertical nystagmus.

Sensory Signs.—One of the most astonishing features of the pontile gliomas in the present series was the practically constant absence of signs of interruption of the sensory pathways. The mesial fillet and the spinothalamic tracts often lay in the midst of the infiltrating tumor, yet clinically they gave no signs of involvement. In only 1 of our cases were sensory signs present; in this case there were decreased sensations of touch, pain and temperature over the left side of the face and the right side of the body. In this respect the present series of cases differs radically from that of Horrax. In the latter series 6 of the 15 patients showed disturbance of sensation involving the trunk, arm and leg but sparing the face. The reason for this difference is not clear.

Signs of Increased Pressure.—These were usually lacking in our series of pontile gliomas. In only 1 case was there papilledema; in 10 of the 11 cases the disks were flat. The spinal fluid pressure was recorded in only 3 instances; in 2 of these it was normal and in the other it was elevated (230 mm. of water) in the presence of flat disks. Usually, roentgenographic evidence of increased pressure was lacking. In 1 case there were marked convolutional atrophy and separation of the sutures; in another the sutures were separated, and in still another there were slight convolutional atrophy and slight separation of the sutures. In the majority of cases, however, roentgenographic studies of the skull showed no evidence of increased intracranial pressure.

PATHOLOGIC PICTURE OF PONTILE GLIOMAS

Gross Features.—Gliomas of the pons invariably cause enlargement of the pons, of greater or lesser degree. This enlargement can be

detected easily on inspection, because the pons is usually a third or a half larger than normal. In a few instances the pons is only slightly enlarged, as in cases 6 and 7. It is usually twisted and turned on its long axis because of the cramped quarters in the posterior fossa caused by the enlarged pons (fig. 1). The surface of the pons is verrucose, lobulated and wartlike. The groove of the basilar artery is usually much deepened. Sometimes overhanging bits of tumor can be seen projecting beyond the edge of the pons. Often the medulla also is enlarged. Sometimes only one side is enlarged; usually the enlargement is symmetric. Occasionally a large, knoblike mass of tumor can be seen projecting from one side of the medulla (fig. 2). Sometimes the mesencephalon is enlarged. This is seen externally in bulging of the cerebral peduncles. Often part of the tumor extends into the cerebellopontile angle; indeed, in the experience of some investigators this occurs in every case (Buckley[4]).

The pons is usually firm and hard on its external surface. Rarely it may be soft, as in case 7, in which the pons was not much enlarged and felt soft, as in a case of vascular softening. The cut surface is firm and often rubbery.

The cranial nerves of the pons and medulla are usually seen lying in the midst of the tumor. The nerves most commonly affected are the trigeminal, the abducens and the facial, but the oculomotor, the auditory and the vagus nerve are sometimes involved also. The nerves of one side are usually more involved than those of the other. This surprising feature was noted also by Buckley in his extensive study of tumors of the pons. As a rule the nerves may be seen lying within the tumor, but in some instances infiltration of tumor into the nerve itself can be seen. This occurred in a case in which there was a small, knoblike swelling of one oculomotor nerve (fig. 3), and in case 9, in which a similar infiltration of the trigeminal nerve was seen (fig. 4). It was observed also in 2 of the cases reported by Buckley. Many of the nerves which appear to be involved in the tumor give no clinical signs of involvement.

Section of the brain usually shows that the greatest infiltration is in the basis pontis. This part of the pons is greatly enlarged, and the markings of the pyramidal and corticocerebellar fibers are much less clear than normal. Not infrequently the tegmentum of the pons is also invaded. In 6 of the 11 cases both the basis and the tegmentum were invaded. In 2 cases the tegmentum was invaded more than the basis, but the latter was also invaded. In 2 other cases the basis was more invaded than the tegmentum, the latter being but little involved. In another case the basis was invaded almost exclusively.

4. Buckley, R. C.: Pontile Gliomas, Arch. Path. **9**:779 (April) 1930.

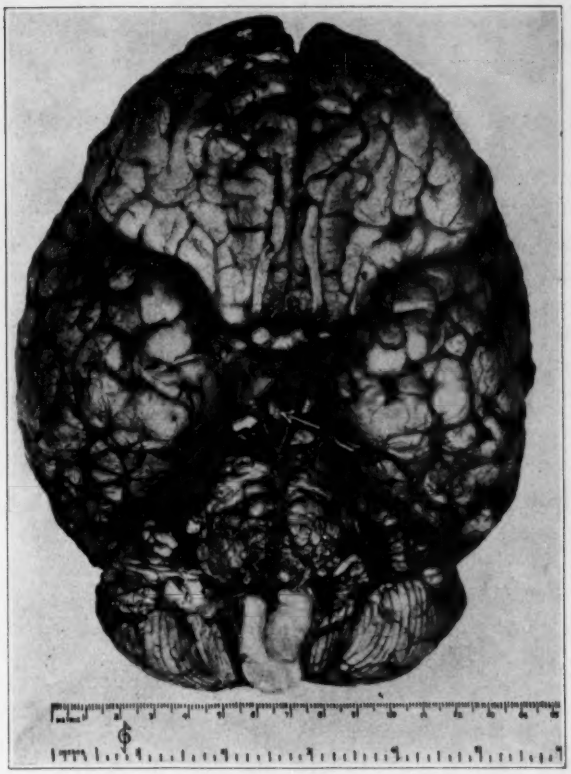


Fig. 3.—Pontile glioma which has extended into the mesencephalon. The arrow points to a nubbin of tumor within the sheath of the right oculomotor nerve. The pons is not much enlarged.

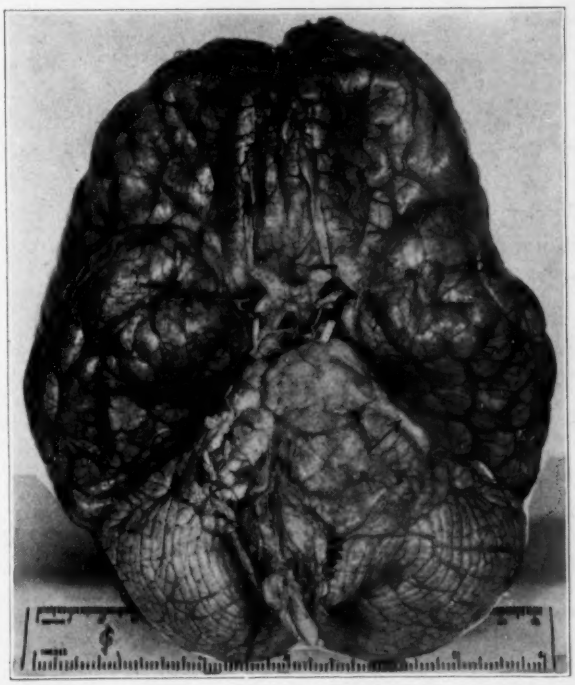


Fig. 4.—Thickening of the left trigeminal nerve, caused by infiltration of the nerve sheath by cells.

The form of extension of pontile gliomas into the medulla and mesencephalon is unpredictable. There is usually extension into the medulla (6 cases) and, more rarely, into the mesencephalon. The extension into these parts of the brain stem may be diffuse and may cause enlargement of the entire medulla or mesencephalon. Usually, however, there is extension by a tonguelike prolongation into one half of the mesencephalon or medulla. This explains the unilateral cranial nerve signs associated with pontile gliomas. The involvement follows no definite pattern; there may be infiltration of almost any part of the medulla or mesencephalon, giving rise to bizarre clinical and pathologic pictures.

Internal hydrocephalus is usually absent. When present it is moderate or mild. This is surprising in view of the compression of the fourth ventricle and the iter by these tumors. These structures often appear to be completely compressed and reduced to a mere slit, but hydrocephalus is usually not present, despite the apparent obliteration of the spinal fluid pathways.

Microscopic Features.—A surprising number of pontile gliomas belong to the glioblastoma multiforme group. In 10 of Buckley's series of 25 cases, the tumor was of this type. Four of the present series were glioblastomas. This is not surprising in view of the rapid clinical course of most of these tumors. The next most common type of glioma observed in the pons is the astrocytoma. This occurred more often than the glioblastoma in the present series (7 cases) but was less frequent in Buckley's series. Spongioblastoma polare has also been observed in the pons (Pilcher [5]); according to Bailey,[6] many pontile gliomas fall into this group. In the infiltrated regions of the pons, medulla or mesencephalon one usually sees many intact axis-cylinders among the infiltrating tumor cells. There is usually more or less complete demyelination of the fibers, but the Bielschowsky stain shows healthy axis-cylinders (fig. 5). This is true also of the infiltrated portions of the tegmentum. These intact axis-cylinders explain the fact that a completely infiltrated region, such as the basis pontis, may give rise to only mild or moderate signs referable to the pyramidal tract or to the cerebellar pathways. Infiltration does not necessarily imply destruction of all the elements in the infiltrated area.

The signs of involvement of the cranial nerves produced by pontile gliomas are the result of nuclear destruction, nerve destruction within the pons or other parts of the brain stem or infiltration of the nerve itself in its peripheral course. Of these mechanisms nerve destruction

5. Pilcher, C.: Spongioblastoma Polare of the Pons: Clinicopathologic Study of Eleven Cases, Arch. Neurol. & Psychiat. **32**:1210 (Dec.) 1934.

6. Bailey, P.: Concerning Diffuse Pontine Gliomas in Childhood, Acta neuropath. **60**:199, 1935.

Fig. 5 (case 5).—Destruction of almost the entire basis pontis and compression and distortion of the tegmentum by a glioma.

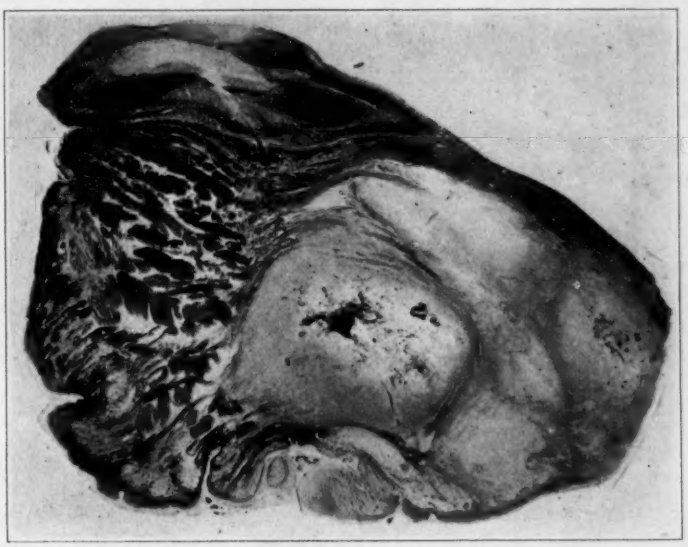


Fig. 6 (case 11).—Unilateral destruction of the base of the pons. The absence of signs referable to the cranial nerves is explained by the lack of infiltration in the tegmentum.

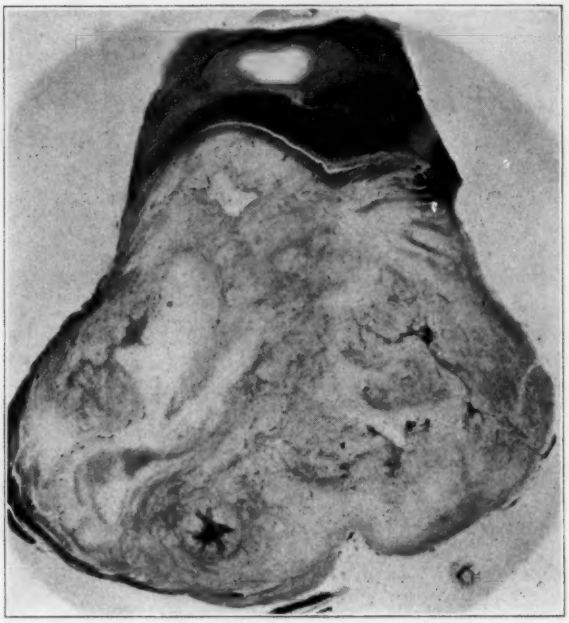


Fig. 7 (case 2).—Invasion and destruction of the entire base of the pons and distortion of the tegmentum.

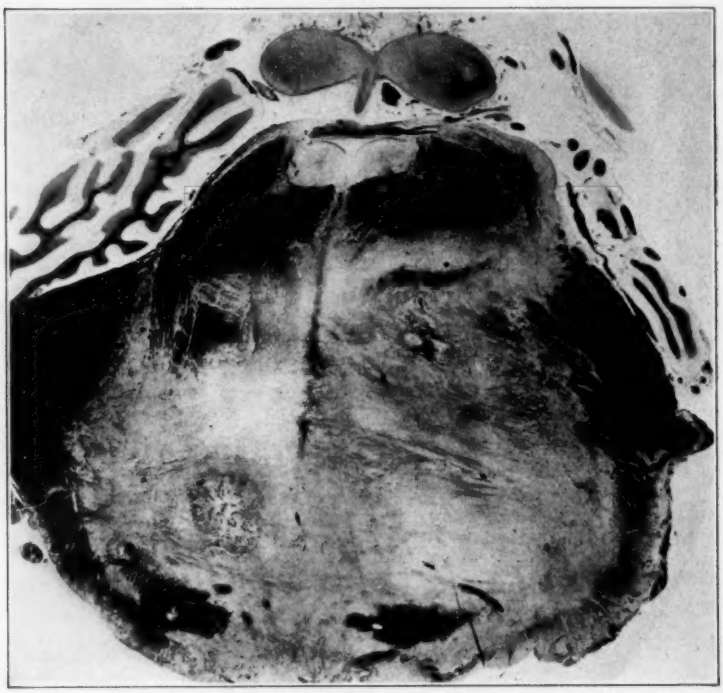


Fig. 8 (case 7).—Partial destruction of the base and tegmentum of the pons by a very soft tumor. There was peripheral facial paralysis in this case. The facial nucleus was destroyed.

is the most common. Nuclear destruction can be seen, but it is not often the cause of the cranial nerve signs. Pontile tumors do not often extend directly into the nuclei of origin of the affected cranial nerves.

Usually, a pontile glioma is confined to the brain stem, but in some cases it extends into the cerebellum. This extension takes place by way of the middle cerebellar peduncle. Most of the cerebellar signs are caused by involvement of the cerebellar pathways in the basis pontis and by involvement of the middle cerebellar peduncle.

DIAGNOSIS

The diagnosis of pontile glioma often is easily made, but sometimes offers serious difficulties. In a typical instance the tumor develops in a child up to 11 or 12 years of age. The onset is often accompanied by diplopia and headache, followed in a relatively short time by paralysis of the cranial nerves (facial, trigeminal and vagus) and by symptoms referable to the cerebellar pathways and to the pyramidal tract. All these develop more or less rapidly during an average course of about three months. Examination reveals paralyses of the cranial nerves, with involvement usually of the abducens, facial and trigeminal and sometimes of the auditory, vagus, hypoglossal and oculomotor nerves. The paralyses are usually unilateral, but may be bilateral. There are almost always some evidence of involvement of the pyramidal tracts (hemiparesis, quadriplegia or even monoplegia) and variable cerebellar signs. Sensory disturbances are strikingly absent in practically every case. Signs of increased pressure are usually absent; choked disk is present in only a small number of cases, and the spinal fluid pressure may be normal. In such a case the clinical picture is that of a process involving the base of the brain, progressive and unaccompanied by signs of increased intracranial pressure. In a typical case there are signs referable to the cranial nerves, to the pyramidal tract and to the cerebellar pathways. In other instances the cranial nerve signs are the outstanding feature and may not be accompanied by other signs or by evidences of pyramidal or cerebellar involvement. Hemiplegia alternans may be helpful in localizing the disease in the pons, but it is not commonly encountered, judging by the present study. When found, it constitutes indubitable evidence of a pontile lesion. In the last analysis the diagnosis of a pontile glioma is made on the basis of progressive involvement of the brain stem, including the various structures indicated. Such a progressive course is improbable in an inflammatory process, though it is possible. It is usual to observe the development of signs while the patient is under observation. In a few of the cases recorded in which the diagnosis of tumor was doubtful, the development of signs and other disturbances while the patient was under observation clinched the diagnosis.

A glioma confined to the dorsal part of the pons offers a particularly difficult problem in diagnosis. That such a localization is possible is shown by some of the cases in the present series and by 4 of Buckley's cases. The diagnosis in such a case is difficult becaue the signs are limited almost entirely to paralyses of the cranial nerves, which may not be numerous. In addition, there may be vague signs affecting other systems, but they are usually so indefinite as to make interpretation difficult. In order to simplify the diagnosis of tumors confined to the dorsal portion of the pons, Rasdolsky [7] described a new symptom complex sometimes encountered with tumors in this area. It was not observed in the present series. The syndrome consists of spasm of the masseter muscle on the side of the tumor, accompanied sometimes by contracture and paresis of the facial muscles of the same side. Spasm of the masseter muscle leads to characteristic difficulty in opening the mouth, causing disturbance in feeding and talking. A patient with such a syndrome talks through the teeth. There is no atrophy of the masseter muscle, and the syndrome has not been observed in cases of tumor in the base of the pons or in other parts of the brain or brain stem. The differential diagnosis includes a consideration of encephalitis, disseminated encephalomyelitis, multiple sclerosis and syphilis of the central nervous system. The progressive nature of the disorder and the absence of fever are of help in differentiating the process from encephalitis of undetermined origin.

Furthermore, the history of onset with diplopia due to paralysis of the external rectus muscle is of great importance in the diagnosis, especially when this diplopia is followed by other evidences of involvement of the brain stem. It is well known that in cases of tumor of the brain with greatly increased intracranial pressure there may be unilateral or bilateral paralysis of the external rectus muscle. This occurs in cases in which there is much pressure and usually late in the course. In cases of pontile gliomas the onset with paralysis of the external rectus muscle as the first sign, in contrast to the late development of this paralysis in cases of tumor causing increased pressure, is of great importance in the differential diagnosis.

Occasionally the diagnosis is rendered more difficult by the history of onset of symptoms following "grip," sore throat or some other infection. Such a history usually leads to the assumption that encephalitis is present, but the diagnosis is eventually clarified by the steady progression of the clinical picture. The occurrence of pyramidal and cerebellar signs is much less likely in the case of encephalitis than in that of tumor. These long tracts are more apt to be involved in disseminated encephalo-

7. Rasdolsky, I.: Syndrome of Neoplasm in the Dorsal Part of the Pons, Ztschr. f. d. ges. Neurol. u. Psychiat. **152**:530 (April) 1935.

myelitis than in other forms of inflammatory disease involving the base of the brain, but the course of this disease should differentiate it easily from a pontile glioma. In such a case there will be evidence of diffuse involvement of the central nervous system beyond the confines of the pons.

Sometimes the differentiation of a pontile glioma from a tumor of the cerebellopontile angle is difficult. In 1 of the cases reported operation was performed, but no tumor of the angle was seen. Horrax and Buckley [8] had a similar experience. Careful analysis of the evidence should make the diagnosis possible. There is usually incomplete involvement of the cochlear nerve; the results of the Bárány test are generally reported as atypical, even though they point to a tumor of the angle, and the history is not that of either an acoustic neuroma or a lesion of the cerebellopontile angle. In the series of cases studied by Horrax and Buckley it was found that pontile tumors do not follow the definite course of acoustic tumors. The onset with deafness, which is so striking a characteristic of acoustic tumor, is much less evident in cases of pontile tumor. When deafness is associated with a pontile tumor it is apt to be less complete than that associated with an acoustic tumor. Mention has been made of the fact that the Bárány response does not give the typical formula of an acoustic tumor or a lesion of the cerebellopontile angle. These are almost always reported as atypical and are only suggestive of lesions in the cerebellopontile angle. This experience has been corroborated by Horrax and Buckley. In addition, choked disk is much more likely to be observed in cases of acoustic tumor. It is usually absent in cases of pontile tumor. Despite these features an occasional pontile glioma will be operated on, as in case 2. With careful attention to details, however, unnecessary operation may be avoided.

SUMMARY

Eleven cases of pontile glioma are analyzed from the standpoint of the subjective and objective manifestations of the tumor.

These observations are correlated with the pathologic features of the tumors.

The diagnosis of pontile gliomas is discussed.

8. Horrax, G., and Buckley, R. C.: A Clinical Study of the Differentiation of Certain Pontile Tumors from Acoustic Tumors, Arch. Neurol. & Psychiat. **24**:1217 (Dec.) 1930.

PATHOLOGIC PICTURE OF THUJONE AND MONOBROMATED CAMPHOR CONVULSIONS

COMPARISON WITH PATHOLOGIC PICTURE OF HUMAN EPILEPSY

LINCOLN OPPER, M.D.*
NEW HAVEN, CONN.

In the attempt to throw light on the pathogenesis and therapeusis of epilepsy the use of convulsant drugs in animal experimentation has been extensive. Chief among the convulsants employed have been some forms of absinth and monobromated camphor, their preference being based mainly on the close resemblance of the artificially provoked attack to the genuine one observed in man. Experimental data have been preeminently pharmacologic,[1] biochemical [2] and neurophysiologic.[3] Pathologic changes in the central nervous system have been observed in epileptic patients, but the possibility of changes occurring as the result of convulsions produced in animals has not been thoroughly investigated. The present study was undertaken to explore this possibility. It was hoped that if lesions of the nervous system did occur they could be correlated with the lesions commonly described in human disease. With

---

* Alexander-Brown-Coxe Fellow in Neuropathology, 1936-1937.

From the Department of Pathology, Yale University School of Medicine.

Dr. Edward Kremers, of the University of Wisconsin, furnished me with the substance, which was regenerated from the bisulfite addition product obtained from the thujone fraction of wormwood oil (Artemisia absinthium L). It is part of fraction 59 to 60 C. (at 45 mm.) of the regenerated ketone. According to Wallach, this is essentially (if not entirely) beta thujone.

1. (*a*) Keith, H. M.: Factors Influencing Experimentally Produced Convulsions, Arch. Neurol. & Psychiat. **29**:148 (Jan.) 1933. (*b*) Sparks, M. I.: Experimental Studies of Epileptiform Convulsions, Arch. internat. de pharmacodyn. et de thérap. **33**:460, 1927.

2. Keith, H. M.: Experimentally Produced Convulsions: Effect on Thujone Convulsions of Insulin and of Variations in the Water Content of the Brain, Arch. Neurol. & Psychiat. **33**:353 (Feb.) 1935.

3. Wortis, S. B.: Experimental Convulsive Seizures, J. Nerv. & Ment. Dis. **77**:233, 1933. Pike, F. H.; Elsberg, C. A.; McCulloch, W. S., and Rizzolo, A.: Some Observations on Experimentally Produced Convulsions: Localization of the Motor Mechanisms from Which the Typical Clonic Movements of Epilepsy Arise, Am. J. Psychiat. **9**:259, 1929.

the exception of the work of Surabaschwili[4] on the histologic substratum of experimentally induced epileptic seizures, the literature has thus far been barren in this regard.

EXPERIMENTAL PROCEDURE

Seventeen cats and 7 rabbits were employed in the experiments. A 20 per cent dilution of thujone in propylene glycol and a 10 per cent solution of monobromated camphor in 95 per cent alcohol, as standardized by Wortis, Coombs and Pike,[5] were employed as convulsants. Alternate cats received thujone, which proved to be the more potent and easily injectable of the two drugs, and camphor exclusively. The 7 rabbits used in the second part of the experiment were convulsed with thujone only. As little as 0.1 cc. of this 20 per cent solution of thujone injected into the femoral vein of a cat weighing from 6 to 10 pounds (2.7 to 4.5 Kg.) or into a vein of the ear of a rabbit within the same limits of weight was sufficient to produce immediate and severe convulsions lasting about ten minutes. Almost invariably a condition resembling status epilepticus could be produced by increasing the dose to a maximum of 0.15 cc. per animal. The 10 per cent solution of camphor administered by the same intravenous route provoked seizures in the cats which were no less severe, but were definitely briefer and less repetitious. The dose for a severe convulsion averaged 0.04 cc. of the standardized alcoholic solution of monobromated camphor per pound of cat. This substance, as already indicated, owing to its tendency to become precipitated by the blood stream and to produce venous thrombosis which frequently suppurated at the site of injection, was not as satisfactory as the thujone in propylene glycol. The latter substance does not injure the walls of the blood vessels and does not induce clotting.

The plan adhered to as closely as possible was to space the injections of the drugs so that a period adequate for complete recovery from the effects of the last dose could be assured between successive convulsions. As the animal would remain apathetic and without appetite for a full day following a severe episode, the necessary period of recovery was regarded as at least two days. Detailed descriptions of the type of clonic-tonic attack elicited by both drugs employed in this experiment have been reported among the observations of other workers.[5] Opisthotonos, pupillary dilatation, cyanosis, sweating of the paws, chewing movements of the jaws, biting of the tongue, loss of sphincter control, yowling and priapism were present to a variable extent during the height of the seizures. Cortical blindness, dyspnea and involuntary running movements always followed the clonic outbursts. In general, it was observed that status epilepticus, lasting from ten to thirty minutes, was more easily produced in rabbits than in cats. The ability to undergo oft repeated injections without suffering the ill effects of prolonged apathy was also more pronounced in rabbits.

Acute and chronic experiments (tables 1 and 2) were conducted, in order to correlate the type and degree of damage to the nervous system with the time and number of convulsions. Rabbits as well as cats were used, to determine a possible species difference in response to the convulsants. With a few exceptions,

4. Surabaschwili, A. D.: Ueber das histologische Substrat der experimentellen (Absinth)- Epilepsieanfälle, Monatschr. f. Psychiat. u. Neurol. **90**:221, 1935.

5. Wortis, S. B.; Coombs, H. C., and Pike, F. H.: Monobromated Camphor: A Standardized Convulsant, Arch. Neurol. & Psychiat. **26**:156 (July) 1931. Sparks.[1b]

TABLE 1.—*Camphor and Thujone Convulsions in Cats*

Cat No.	Convulsant	Duration of Experiment, Days	Number of Injections	Number of Convulsions	Time Between Last Convulsion and Autopsy, Days	Relative Histologic Damage	Nature and Site of Microscopic Lesions
1	Camphor	3	3	12	0	++	Irregular staining reaction of nerve cells throughout second and third layers of cerebral cortex; cytoplasmic homogenization of nerve cells in third layer of cortex of occipital lobe; granular cytoplasmic disintegration of nerve cells in cortex of frontal lobe
2	Camphor	5	4	10	0	++	Cortical necrobiosis in frontal and parietal lobes; "wind-blown" appearance of shrunken and hyperchromatic nerve cells in cortex of parietal lobe
3	Camphor	6	3	18	0	+	Shrunken and hyperchromatic cells in third layer of cortex of parietal lobe; granular cytoplasmic disintegration of nerve cells in cortex of frontal lobe
4	Thujone	8	4	4	2	++	Necrobiosis in cortex of frontal lobe
5	Thujone	9	4	4	0	+++	Fresh focal hemorrhage in cerebellar cortex; hyperchromatic ganglion cells in cortex of parietal lobe
6	Camphor	10	5	15	0	+	Necrobiosis in cortex of parietal lobe; irregular staining reaction of cells in second and third cortical layers of temporal lobe
7	Thujone	11	4	4	0	+++	Fresh focal hemorrhage in cortex of parietal lobe; cytoplasmic homogenization and loss of Nissl apparatus in nerve cells of third layer of cortex of temporal lobe
8	Thujone	11	4	4	2	++	Necrobiosis and hyperchromatic ganglion cells in cortex of frontal and of temporal lobe
9	Camphor	11	2	1	7	+	Small patch of necrobiosis involving motor cells of cortex
10	Camphor	12	4	7	5	+	Hyperchromatic ganglion cells in cortex of temporal lobe
11	Camphor	13	4	14	5	++	Hyperchromatic ganglion cells with corkscrew processes in subiculum
12	Camphor	14	2	6	5	++	Patchy necrobiosis and hyperchromatic shrunken nerve cells in third, fourth and fifth cortical layers of frontal, of temporal and of parietal lobe
13	Camphor	26	3	7	17	++	Shrunken and hyperchromatic cells in cortex of temporal and of parietal lobe
14	Camphor	52	2	11	47	++	Areas of necrobiosis in cortex of temporal and of parietal lobe
15	Camphor	67	3	5	50	+	Few small areas of necrobiosis in cortex of frontal and of parietal lobe
16	Thujone	90	4	4	81	+	Necrobiosis; hyperchromatic and pale ganglion cells in cortex of frontal lobe
17	Thujone	94	4	4	85	No changes	

in which the severity of the repeated seizures had a rapidly fatal outcome, none of the animals died spontaneously. Chloroform was used, and autopsy followed death by never more than an hour. Numerous blocks of brain and cord were placed in 95 per cent alcohol and stained with toluidine blue according to the method of Nissl. Supplementary staining for glial fibers by the Victoria blue or Holzer method was employed in many cases. The attempt was made to disclose significant intraganglionic fibrillary changes by the Bielschowsky technic. The visceral organs of all rabbits were examined microscopically after fixation with Zenker's solution (prepared with acetic acid) and staining with Delafield's alum-hematoxylin stain and eosin.

TABLE 2.—*Camphor and Thujone Convulsions in Rabbits*

Rabbit No.	Convulsant	Duration of Experiment, Days	Number of Injections	Number of Convulsions	Time Between Last Convulsion and Autopsy, Days	Relative Histologic Damage	Nature and Site of Microscopic Lesions
1	Thujone	1	1	1	1	+	Small area of necrobiosis in cortex of frontal lobe
2	Thujone	9	4	4	2	+	Necrobiosis and shrunken hyperchromatic ganglion cells in cortex of frontal lobe
9	Thujone	9	4	4	4 hrs.	+	Necrobiosis in cortex of parietal lobe
4	Thujone	10	4	4	0	++++	Degeneration of nerve cells and reparative glial proliferation throughout entire cerebral cortex; chromatolysis of Purkinje cells; extensive patchy fibrosis throughout cardiac muscle; chronic passive congestion of liver
5	Thujone	23	4	4	0	+	Necrobiosis and hyperchromatic ganglion cells in cortex of frontal and of parietal lobe
6	Thujone	25	10	10	0	++	"Wind-blown" appearance of shrunken cells in cortex of parietal lobe; cortical necrobiosis in temporal lobe; mild gliosis surrounding Purkinje cells
7	Thujone	33	5	5	10	++	Shrunken and hyperchromatic ganglion cells in third cortical layer of temporal and of parietal lobe

RESULTS

Grossly, autopsy revealed no changes in the central nervous system of any of the animals. Microscopically, the cerebral changes, which in general were more striking qualitatively than in their extent, were best demonstrated by the Nissl method. In spite of careful histologic study, the spinal cords appeared uniformly normal.

From the tables it may be seen that autopsy was performed either at once after a final severe convulsion or from one to eighty-five days following the last attack. A clearcut difference in the nature of the lesions was evident on the basis of the interval between the last con-

vulsion and the autopsy. The extent of the lesions in most animals was less clearly dependent on the number and intensity of the seizures. This was striking in cats 3, 6, 10 and 17 and in all the rabbits with the exception of no. 4. An explanation for this appears to lie in the great reversibility of the acute changes.

To be regarded as vestiges of one or more remote attacks were the necrobiosis and the sclerosis of the ganglion cells, changes familiar to students of human epilepsy. Simple disappearance of nerve cells in focal zones throughout the cerebral cortex was most commonly encountered. This cortical necrobiosis appeared in the form of discrete acellular patches in 9 cats and 5 rabbits (fig. 1 *A*). Almost as common as the necrobiotic lesions and involving larger cortical zones were sclerotic, hyperchromatic nerve cells, generally acknowledged to represent a chronic type of injury. Spielmeyer [6] expressed the opinion that such cells persist in the cortex without functional capacity. These cells were noted in the cerebrums of 9 cats and 4 rabbits and frequently lay adjacent to necrobiotic foci (fig. 1 *B*). Characteristic of the change was the conversion of the normal ganglion cells to shrunken, darkly staining forms in which the nuclei could not be distinguished. The pathologically altered cellular processes, traceable over long distances in the preparations, sometimes assumed corkscrew-like configurations, as in cat 11 (fig. 2 *A*).

By far the most extensive damage to cerebral tissue was seen in rabbit 4. This animal was unique in several respects. The number of injections and convulsions which marked its course of ten experimental days was equaled by 3 and surpassed by 2 other animals of this series of 7 rabbits. Yet it is worthy of some consideration that the status epilepticus after the first injection of thujone lasted the unusual period of one hour and fifteen minutes and that for some hours following this cyanosis was extreme, respirations were weak and the animal appeared moribund. Moreover, at the last injection, ten days later, the animal reacted to the thujone with a single, brief convulsion and immediate spontaneous death. The histologic change was in the nature of widespread degeneration of nerve cells, with liquefaction and chromatolysis, most conspicuous in the three superficial cortical layers. A progressive glial reaction was marked by the proliferation of fibrous astrocytes and Hortega cells (fig. 2 *B*). Regressive forms could be seen in the numerous swollen ameboid cells. More surprising than the extent of the cerebral involvement was the concomitant pathologic alteration of the heart and liver. The entire cardiac muscle was checkered with focal areas of active fibrosis (fig. 2 *C*). The liver showed acute

6. Spielmeyer, W.: Histopathologie des Nervensystems, Berlin, Julius Springer, 1922.

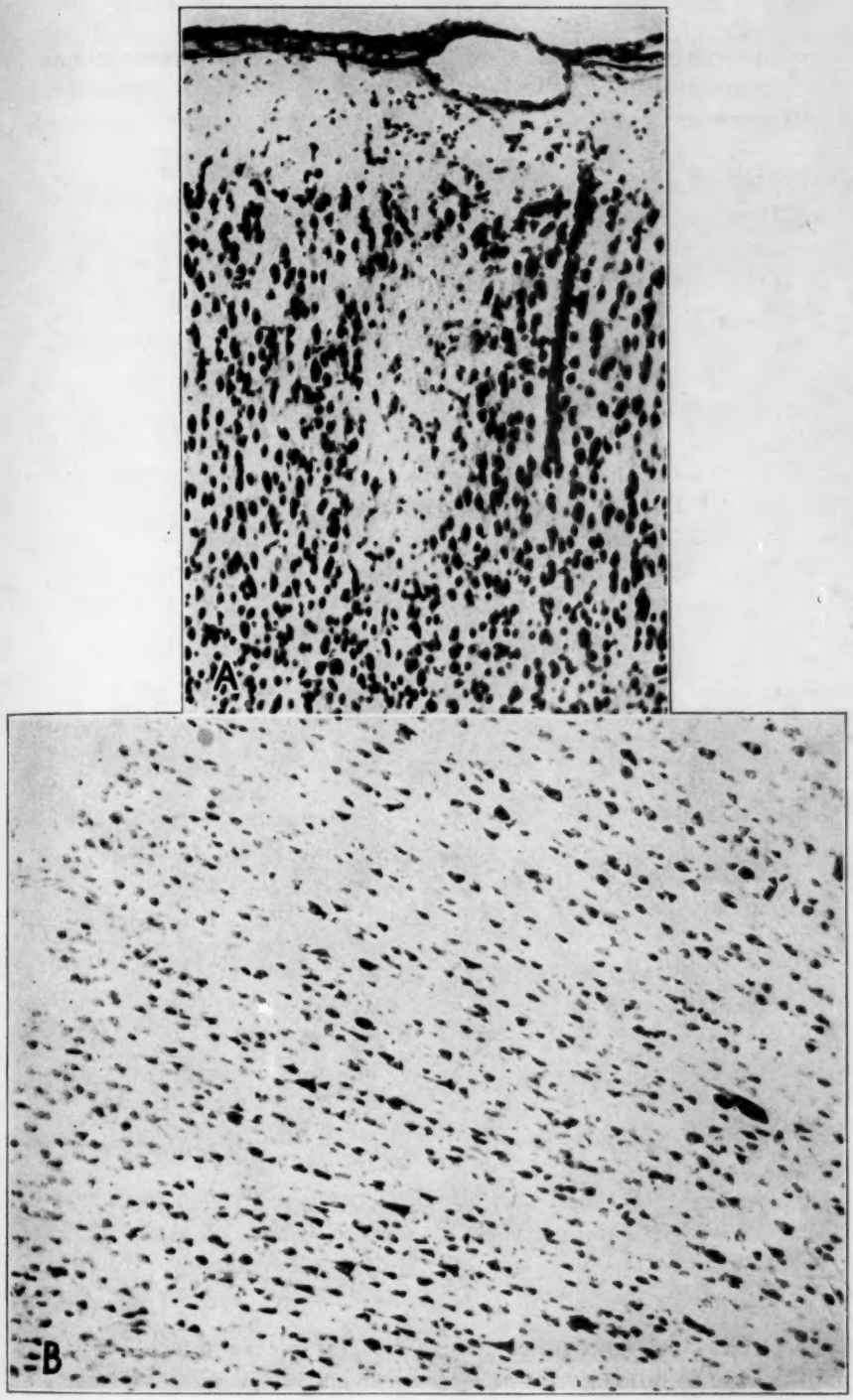


Fig. 1.—*A*, "punched-out" zone of necrobiosis in cortex of temporal lobe of rabbit *6*. Nissl stain; × 100. *B*, shrunken hyperchromatic ganglion cells in cortex of parietal lobe of cat 12. Nissl stain; × 125.

passive congestion, with early fibrosis in the central necrotic zones. From the clinical course and the appearance of the lesions it seemed that the processes in the brain and heart had been precipitated simultaneously

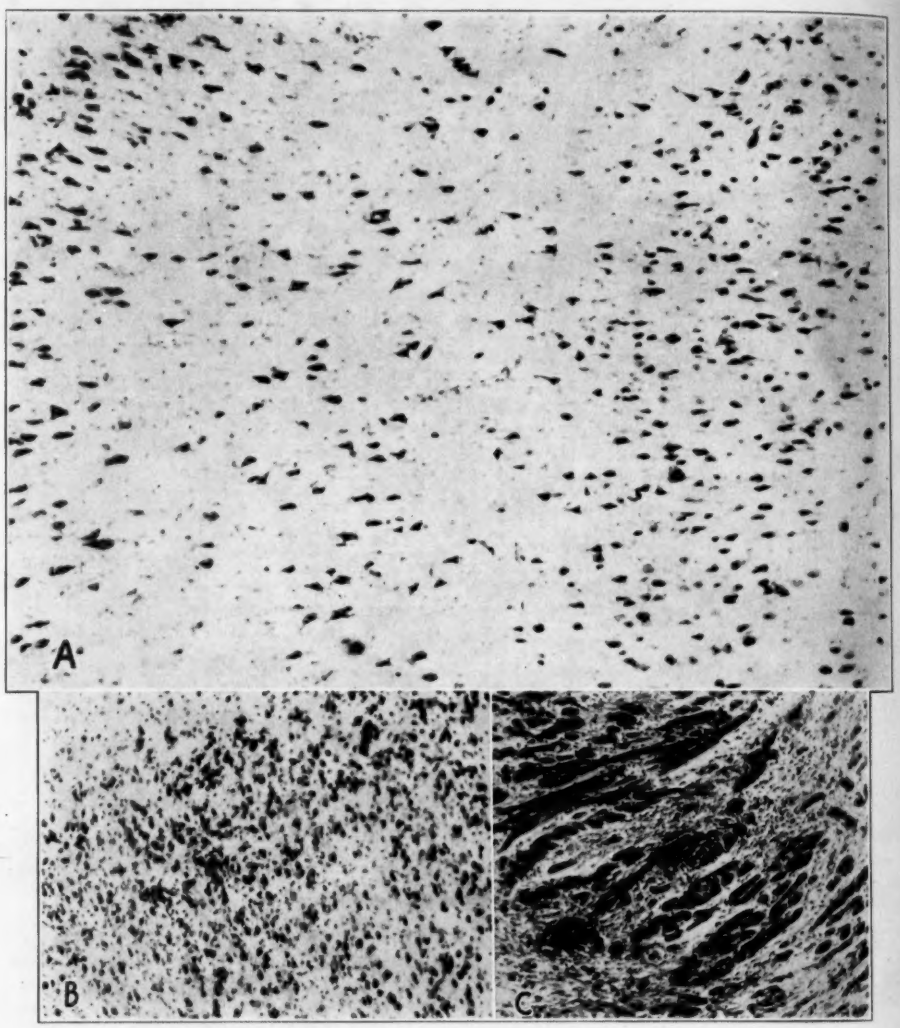


Fig. 2.—*A*, sclerotic ganglion cells in subiculum of cat 11. Nissl stain; × 125. *B*, degeneration of cortical ganglion cells and glial proliferation in parietal lobe of rabbit 4. Nissl stain; × 66⅔. *C*, myocardial fibrosis in rabbit 4. Hematoxylin and eosin; × 66⅔.

by the first series of convulsions and that the unexpected fatal response to the last injection was due to cardiac failure.

Acute lesions were of several varieties and appeared only in cases in which the experiments were terminated within a few hours after a

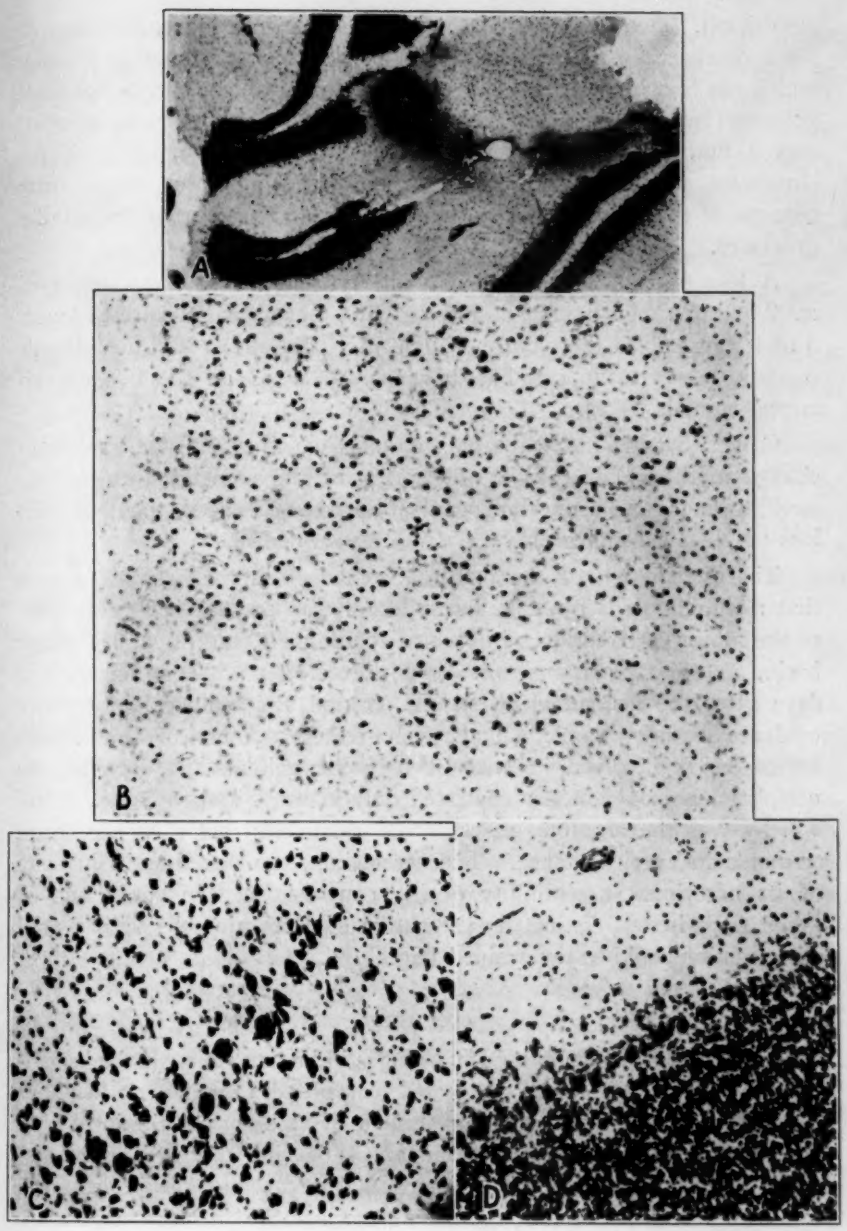


Fig. 3.—*A*, hemorrhage in cerebellar cortex of cat 5, showing destruction of granular and molecular layers. Nissl stain; × 23½. *B*, irregular staining of cortical ganglion cells of cat 1. Nissl stain; × 98. *C*, cytoplasmic hemogenization of cortical motor cells in cat 1. Nissl stain; × 78. *D*, disintegration of several Purkinje cells and replacement by glial elements in rabbit 6. Nissl stain; × 78.

convulsion. Two animals, cats 5 and 7, showed fresh hemorrhages in the cerebellar and the parietal cortex, respectively (fig. 3 *A*). A lesion which can best be described as irregular staining of nerve cells and their processes was observed in the second and the third cortical layer of cats 1 and 6 (fig. 3 *B*). Characteristic were the clumping of the chromatin and the disappearance of the Nissl apparatus, the angular contour of the cells and the curious swelling and beading of the cellular processes.

A loss of cellular polarity was observed in the cerebral cortex of cat 2 and of rabbit 6. The resulting "wind-blown" appearance of layers 3 and 5 resembled the picture of dementia paralytica. No such chronic process, however, appeared to have played a role in the two experimental animals.

Cats 1, 3 and 7 were the only animals which revealed a significant change in the motor cells of the cortex of the frontal lobe. Cellular swelling and cytoplasmic homogenization were observed, together with loss of Nissl substance (fig. 3 *C*).

The distribution of the pathologic changes in the brain was such that a minimum of one significant lesion was present in at least one of the major cerebral lobes in each of the animals, except cat 17, whose brain, in spite of four convulsions, revealed no change eighty-five days after the last attack. Parietal, frontal and temporal lobes bore evidence of microscopic damage the greatest number of times, each region being involved in at least half the animals. Lesions of the occipital lobe could be demonstrated only in cat 1 and rabbit 4. Noteworthy was the absolute intactness of Sommer's sector of the cornu ammonis in every instance. The cerebellum, too, fared well, in spite of its notorious susceptibility during convulsions.[7] In cat 5 and in rabbit 6 slight but distinct disintegration of Purkinje cells with a mild glial reaction could be determined (fig. 3 *D*).

COMMENT

Compared with the pathologic changes in human epilepsy, the experimentally produced lesions revealed certain differences as well as similarities. Most familiar to the student of epilepsy are the local phenomenon of sclerosis of the cornu ammonis and, more diffusely distributed over the entire cerebral cortex, the marginal gliosis described by Chaslin. Bratz [8] and Spielmeyer [7] described the former condition in

7. Spielmeyer, W.: The Anatomic Substratum of the Convulsive State, Arch. Neurol. & Psychiat. **23**:869 (May) 1930.

8. Bratz: Das Ammonshorn von Epileptischen, Paralitikern, Senildementen und anderen Hirnkranken, Monatschr. f. Psychiat. u. Neurol. **47**:56, 1920.

50 per cent of their cases; Tramer [9] observed the latter in most of his cases. In my experiments with 24 animals the cornu ammonis was completely spared, and only rabbit 4 disclosed an increase in horizontal fibrous glia, particularly in the molecular layer of the cerebral cortex. The patches of necrobiosis and the sclerotic changes in the cells which were present in abundance in these animals have been described frequently in epilepsy.[7]

Following status epilepticus in man, in the absence of other vascular changes [10] there is often bleeding into the leptomeninges and cerebral parenchyma, comparable to the situation in 2 of my animals. As the cause of death, petechiae in the vicinity of the nuclei of cranial nerves have been both assumed clinically and ascertained at necropsy. Other acute alterations of nerve cells, such as cytoplasmic homogenization and loss of Nissl substance, have been observed repeatedly in human beings after seizures.[11] Entirely analogous to the condition of rabbit 4, whose heart was simultaneously involved with the cerebral process, was that reported by Grüber and Lanz.[12]

The zonal loss of cellular polarity, the picture of coarsely granular disintegration and swelling of individual cells and the irregular staining properties of cells in the second and third cortical layers noted in my animals are not reconcilable with the picture of human epilepsy. Closely resembling the poor staining properties of the cortical ganglion cells in my animals was the "toxic effect of absinth" noted practically throughout the entire cortex of several of Surabaschwili's [4] dogs. Surabaschwili stated that this histologic change was the direct toxic effect of the noxious agent absinth, but there is evidence neither for nor against this belief.

Spielmeyer's widely accepted "vascular" or "vasospastic" conception of epilepsy is based partially on the ischemic nature of the lesions and partially on their localization in the poorly vascularized Sommer sector of the cornu ammonis.[13] The regular absence of lesions in the Sommer sector in my animals would seem to be the strongest argument against the possibility that vascular spasm produced the experimental epileptiform seizures. Conceivably, however, there may be a more generous supply of blood to the cornu ammonis of rabbits and cats than of man.

---

9. Tramer, M.: Untersuchungen zur pathologischen Anatomie des Zentralnervensystems bei der Epilepsie, Schweiz. Arch. f. Neurol. u. Psychiat. **2**:202, 1918.

10. Alquier, L., and Anfimow, W.: Existence et signification de petites hémorragies sous la pie-mère cérébrale dans l'épilepsie, Rev. neurol. **15**:89, 1907.

11. Volland: Histologische Untersuchungen bei epileptischen Krankheitsbildern, Ztschr. f. d. ges. Neurol. u. Psychiat. **21**:195, 1914. Spielmeyer.[7]

12. Grüber, G. B., and Lanz, H. F.: Ischämische Herzmuskelnekrose bei einem Epileptiker nach Tod im Anfall, Arch. f. Psychiat. **61**:98, 1919.

13. Uchimura, J.: Ueber die Gefässversorgung des Ammonshorns, Ztschr. f. d. ges. Neurol. u. Psychiat. **112**:1, 1928.

The fibrosis in the cardiac muscle and the concomitant cerebral lesions of rabbit 4 suggest a common vascular basis. Their association in human epilepsy has been held as one of the supports of the vascular theory.[14]

SUMMARY AND CONCLUSIONS

Seventeen cats and 7 rabbits were convulsed with monobromated camphor or with thujone.

In general, the extent of the resulting cerebral lesions was not dependent on the number and intensity of the seizures.

A definite correlation between the recency of the last series of convulsions and the amount of morphologic change in the brain could be demonstrated. Old lesions were not frequently demonstrable because of the reversibility of many of the acute changes.

Lesions were largely confined to the cerebral cortex. The cornu ammonis was spared, and the cerebellum was rarely affected.

Strikingly like the pathologic changes in human epilepsy were the necrobiosis, the sclerosis of the ganglion cells, the petechial hemorrhages and the chromatolysis of the nerve cells.

Many of the lesions suggested, but did not prove, a pathogenesis similar to that which is embodied in Spielmeyer's "vascular" conception of epilepsy.

Histologic study of the pathologic changes which resulted from the experimentally induced convulsions failed to reveal significant species differences between rabbits and cats.

---

14. Spielmeyer, W.: Funktionelle Kreislaufstörungen und Epilepsie, Ztschr. f. d. ges. Neurol. u. Psychiat. **148**:287, 1933.

"SILVER CELLS" AND "SPIROCHETE-LIKE" FORMATIONS

IN MULTIPLE SCLEROSIS AND OTHER DISEASES OF THE CENTRAL NERVOUS SYSTEM

GEORGE B. HASSIN, M.D.
Professor of Neurology, University of Illinois College of Medicine,
Attending Neurologist, Cook County Hospital
AND
ISADORE B. DIAMOND, M.D.
Assistant Professor of Neurology, University of Illinois College of Medicine
CHICAGO

Granules with affinity for silver—silver granules—have been described at various times in pathologic and neuropathologic literature. Thus, Jahnel [1] in 1919 spoke of dark granules which were scattered in the tissues, singly or in connection with threadlike fragments of Spirochaeta pallida. He stated that Levaditi and his co-workers described ultramicroscopic granules which, like Jahnel's granules, represented modified spirochetes. Jahnel saw the granules only in areas densely invaded by spirochetes, but never in areas free from them.

Kon [2] observed silver granules in practically every tissue and organ of the body, including the brain. Fine and coarse black or brown granules were present also in the cytoplasm of the ganglion cells, but not in their nuclei. In the brain of a rabbit "blackish" granules were present in the cortex, optic thalamus, corpora quadrigemina, cerebellum, pons, medulla, spinal cord and sympathetic and spinal ganglia. In the nuclei of the hypoglossal nerve, "dotlike" blackish granules were scattered over the bodies of the cells, but they did not invade the nuclei. In the nuclei of the vagus nerve granules of the foregoing type were so numerous that they covered the cell nuclei, while in the nuclei of the third nerve the granules were coarse and situated at the periphery. In the human brain the presence of silver granules was demonstrated by Kon and his co-workers within twenty-four hours after death. As the granules disappear after a fresh piece of brain tissue has been in running water for

From the Division of Neuropathology (Dr. G. B. Hassin, Director), Department of Neurology and Neurological Surgery, University of Illinois College of Medicine.

1. Jahnel, F.: Quoted from his Pathologische Anatomie der progressiven Paralyse, in Bumke, O.: Handbuch der Geisteskrankheiten, Berlin, Julius Springer, 1930, vol. 11, p. 513.

2. Kon, Y.: Ueber die Silberreaktion der Zellen, Jena, Gustav Fischer, 1933.

twenty-four hours, it is to be assumed that the substance of the granules, stainable with silver, is not stable. Nor can granules be demonstrated when pieces of brain tissue have been kept in alcohol, solutions of formaldehyde or osmic acid. Though labile formations, the silver granules are, according to Kon, integral parts of the cytoplasm, like Nissl bodies, neurofibrils, plasmosomes, pigment, fat granules or supravital stainable substances; in short, they are specific formations.

A different type of silver granules was described by Steiner. First in collaboration with Kuhn [3] and then for twenty years alone,[4] Steiner studied silver granules in dementia paralytica and multiple sclerosis and their possible origin from spirochetes. Steiner maintained that multiple sclerosis is an infectious disease caused by a specific spirochete, different from any other spirochete—for instance, that of syphilis, of Weil's disease, or of relapsing fever. It is a destroyer of myelin and therefore was termed by him Spirochaeta myelophthora. It is short lived, for it rapidly breaks up into small fragments or granules, which are picked up by glia cells or lymphocytes, resulting in the formation of so-called "silver cells" (argyrocytes).

By a special silver staining method [5] Steiner was able to demonstrate "silver cells" in every case of dementia paralytica and multiple sclerosis;

---

3. Kuhn, P., and Steiner, G.: (*a*) Ueber Ursache der multiplen Sklerose, Med. Klin. **13**:1007, 1917; (*b*) Forschungen über die Aetiologie der multiplen Sklerose, München. med. Wchnschr. **66**:1245, 1919.

4. Steiner, G.: (*a*) Untersuchungen zur Pathogenese der multiplen Sklerose, Zentralbl. f. d. ges. Neurol. u. Psychiat. **47**:701, 1927; (*b*) Demonstration von Spirochäten im menschlichen Gehirn bei multipler Sklerose, Deutsche Ztschr. f. Nervenh. **107**:112, 1928; (*c*) Krankheitserreger und Gewebsbefund bei multipler Sklerose: Vergleichend-histologisch-parasitologische Untersuchungen bei multipler Sklerose und anderen Spirochätosen, Ergebn. d. Hyg., Bakt., Immunitätsforsch. u. exper. Therap. **12**:269-464, 1931; (*d*) Ueber die Ursache der multiplen Sklerose: Entgegnung zu dem Aufsatz von Kuhn, Med. Klin. **30**:269, 1934; (*e*) Spirochäten im menschlichen Gehirn bei multipler Sklerose, Nervenarzt **1**:457, 1928; Neues zur Aetiologie der multiplen Sklerose, ibid. **5**:281, 1932.

5. Formaldehyde-fixed tissue is washed in running water for from two to five hours; frozen sections 60 microns thick are carried into water and placed in 95 per cent alcohol overnight and for one to two minutes in 1 per cent solution of uranium nitrate in dehydrated alcohol (kept in a dark glass-stoppered bottle); they are then washed in two changes of hot water and allowed to remain in a third dish of hot water for one-half hour, placed for five minutes at room temperature in a 1 per cent solution of gum mastic, removed singly with a glass rod rinsed in dehydrated alcohol and rinsed in three changes of water, after which they are placed in 0.1 per cent solution of silver nitrate and heated until steam and bubbles appear. The sections should not be allowed to touch one another. They are allowed to cool for two or three minutes and washed twice in hot water, placed for five minutes at room temperature in the solution of gum mastic and removed again as mentioned before. A mixture of 5 per cent

Spirochaeta myelophthora in 25 per cent of cases of multiple sclerosis and Spirochaeta pallida in every case of dementia paralytica.

Steiner's observations were substantiated, but only as to the presence of silver cells (Nishii,[6] Pette,[7] Marburg,[8] Lüthy,[9] Rogers,[10] Kopeloff and Blackman[11] and Blackman and Putnam,[12] which, however, were observed (Blackman and Putnam [12]) in conditions other than multiple sclerosis and dementia paralytica. Steiner's observations concerning the presence of spirochetes in multiple sclerosis and the possible origin of silver granules from them were confirmed only by Scheinker,[13] who found spirochete-like formations in 4 cases of multiple sclerosis.

Before we proceed with the description of our studies, we wish to outline briefly Steiner's lifelong work, summed up by him in an extensive monograph,[4c] which is not easily accessible.

Steiner emphasized the necessity of using large frozen sections, which must be longitudinal when taken from the spinal cord; their thickness must be 60 microns; in multiple sclerosis spirochetes and silver cells should be looked for in the white substance (not as in dementia paralytica, in the gray substance), at the border of the gray matter, in the subependymal areas and in the adventitial and subarachnoid spaces of Virchow and Robin, where silver cells are seen with especial frequency. Steiner was able to observe within some silver cells fragments of spiro-

---

aqueous solution of pyrocatechin (freshly made) and 4 drops of mastic (3 per cent solution) is heated to the boiling point, and the sections placed therein and allowed to cool for six to eight minutes, washed in two changes of hot water and counterstained in a 1 per cent alcoholic solution of fuchsin, dehydrated in 95 per cent and dehydrated alcohol, cleared in xylene and mounted in balsam. The water used must be double distilled. The gum mastic is made with 95 per cent alcohol (6 per cent) and diluted to the desired degree with dehydrated alcohol.

6. Nishii, R.: Untersuchungen über das Vorkommen von Spirochäten und "minute bodies" bei der multiplen Sklerose, Arb. a. d. neurol. Inst. a. d. Wien. Univ. **31**:153, 1929.

7. Pette, in discussion on Steiner.[4b]

8. Marburg, in discussion on Steiner.[4b]

9. Lüthy, F.: Zur Frage der Spirochätenbefunde bei multipler Sklerose, Ztschr. f. d. ges. Neurol. u. Psychiat. **128**:290, 1930.

10. Rogers, H. J.: The Question of Silver Cells as Proof of the Spirochetal Theory of Disseminated Sclerosis, J. Neurol. & Psychopath. **13**:50, 1932.

11. Kopeloff, N., and Blackman, N.: Silver Cells (Steiner's Method) in Multiple Sclerosis Compared with Their Presence in Other Diseases, Arch. Neurol. & Psychiat. **34**:1297 (Dec.) 1935.

12. Blackman, N., and Putnam, T. J.: Nature of the "Silver Cells" Occurring in Multiple Sclerosis and Other Diseases, Arch. Neurol. & Psychiat. **39**:54 (Jan.) 1938.

13. Scheinker, I.: Ueber Spirochätenbefunde im Zentralnervensystem bei vier Fällen von multipler Sklerose, Wien. klin. Wchnschr. **51**:307, 1938.

chetes, their extracellular portion undergoing degeneration and presenting transitional stages from spirochete to silver cell. Silver cells are thus to be looked on as degenerated spirochetes, representing an advanced stage of a spirochetal infection. Silver cells containing fine granular substance are the older; the fresh, younger cells containing formations in the form of ringlets, commas, loops and rods represent an early stage of spirochetal infection. This accounts for the fact that in dementia paralytica, for instance, areas rich in spirochetes are poor in silver cells and vice versa. In cases in which the course has been rapid and cases of young persons silver cells are numerous; in cases in which the disease is of long duration silver cells are harder to demonstrate; only the fine granules are present, without the clear threadlike argyrophilic content. Steiner emphasized that the silver cells and specimens of Spirochaeta myelophthora are not fragments or fibrils of connective or glial tissue, lipoids, prelipoids, pigment granules or reticulin, some of which may stain deeply with silver nitrate and appear like spirochetes or silver cell granules. In abscess of the brain, tuberculous and septic meningitis and some other conditions, Steiner found no argyrophilic content in the lymphocytes.

OUR OBSERVATIONS

By Steiner's method we studied 24 cases of various organic disorders: multiple sclerosis (8 cases), dementia paralytica, herpetic encephalitis, myelogenic leukemia, myelomalacia, subacute bacterial endocarditis, cerebral hemorrhage, Parkinson's disease, toxemia, astrocytoma, metastatic carcinoma, Friedreich's ataxia and meningioma of the brain. We studied also 1 case of suicide by hanging. We contrasted the changes in our cases with those appearing in the specimens made in cases of dementia paralytica and of multiple sclerosis and placed by Dr. Steiner at our disposal. We did not use large sections, as advocated by Steiner, and the spinal cord was studied in both transverse and longitudinal sections. Especial attention was paid to the condition of the subependymal areas, where, according to Steiner, spirochetes may be found in multiple sclerosis.

Spirochetes in Multiple Sclerosis and Other Conditions.—Neither in the brain nor in the spinal cord in multiple sclerosis did we see spirochetes; in dementia paralytica they could be demonstrated mixed with so-called silver cells. Formations resembling spirochetes, in the form of thick curved short coarse bodies (fig. 1), not unlike those pictured by Steiner, were seen in specimens made in cases of multiple sclerosis, herpetic encephalitis, subacute bacterial endocarditis, myelomalacia, tumor of the brain, Friedreich's ataxia and subacute combined degeneration of the spinal cord. Ringlets, loops and rods were exceedingly

rare. In the spinal cord such formations were numerous in longitudinal sections, where they appeared darkly stained and could be differentiated from connective or glial tissue and other artefacts. It should be emphasized that the formations described—as the photomicrograph and drawings show (figs. 1 and 2)—only look like spirochetes and were by no means typical. As the sections were too thick (60 microns), photomicrographs were not always successful and drawings had to be used (fig. 2).

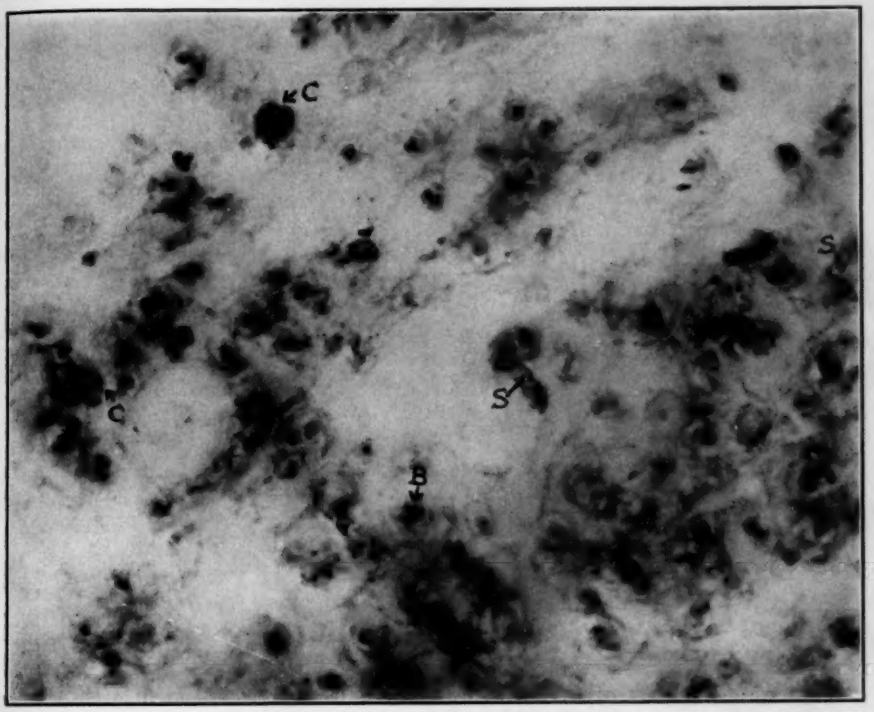


Fig. 1.—Subacute combined degeneration of the cord. At *S S* a curved spirochete-like darkly stained structure can be discerned; at *B* is a similar, less distinct formation; *C C* show silver cells, better pictured in figure 4. Numerous granules, mostly intracellular, can be seen scattered through the section. Other formations are reproduced as drawings in figure 2.

Silver Granules and Cells.—Silver granules were present in all the 8 cases of multiple sclerosis studied. They were numerous in the areas bordering on the plaques (fig. 3, *2*), the so-called transitional or intermediate areas of sclerosis in which the degeneration of the nerve fibers has not reached the final stage, that of plaque formation. They were less numerous in the apparently normal-looking areas (fig. 3, *3*) and were exceptionally rare and often absent in the patches themselves (fig. 3, *1*).

The granules were gathered around a central core (fig. 4) which was homogeneous in appearance and structure; that is to say, it never exhibited granules suggestive of a lymphocyte or glia cell. In the sections of the spinal cord cut transversely, these structureless pale oval or round bodies were enveloped by a black granular membrane and impressed one as cells containing silver granules, that is, as silver cells. Near the adventitial spaces of arteries, veins or capillaries such "silver cells" were often gathered in large numbers and, owing to the thickness of the sections, often seemed to appear above the smaller blood vessels and capillaries. By turning the micrometer it was possible to demon-

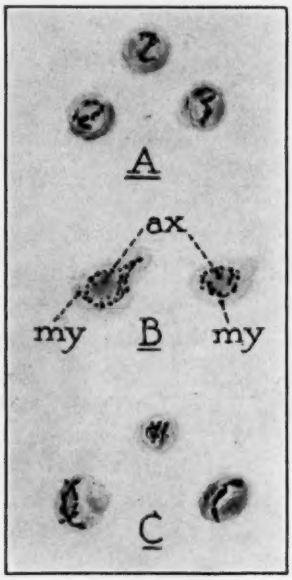


Fig. 2.—Spirochete-like formations and silver cells. *A* is a section from the spinal cord in a case of Friedreich's ataxia; *B* shows silver cells in a section made in a case of multiple sclerosis; *C* is a section made in a case of myelomalacia. The silver granules are situated between the axon (*ax*) and the myelin (*my*) which is as a faint ring requiring use of a hand lens.

strate that the silver granules or cells often had no connection with the blood vessels. Wherever situated, the silver granules, as has been stated, always surrounded or enveloped an oval homogeneous body which impressed one at first glance as a nucleus. In some cases, especially when counterstained with fuchsin, it was possible to show clearly that the silver granules lay between the axon and myelin, where they occupied a space assigned to the so-called Mauthner membrane, as if dividing the axon from the myelin sheath (fig. 2 *B*).

Black granules were also seen, often in large numbers, in and around amyloid bodies; in the white corpuscles within the capillaries; around or among the red corpuscles; in the adventitial and endothelial cells; in the gray substance of the spinal cord, the anterior commissure, the central canal of the spinal cord and in the anterior and posterior roots, where they were large and arranged singly or in foci. Silver granules were not seen in gitter cells, but minute dotlike black granules were scattered over areas that appeared normal.

In longitudinal sections of the spinal cord the silver granules were arranged in the form of threads along the course of the axons and often gave the impression of corkscrew bodies resembling spirochetes. They

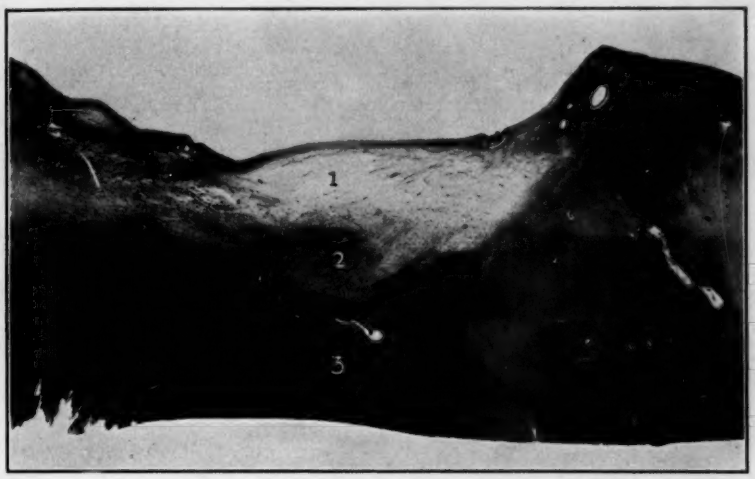


Fig. 3.—A periventricular plaque (*1*) around the anterior horn of the lateral ventricle in a case of multiple sclerosis. At *2* the transitional zone can be seen, and at *3* normal-looking tissue is present (Steiner's stain).

were also present in the subarachnoid spaces, especially the cerebral ones, where they appeared much smaller and always densely stained.

As has been mentioned, we saw silver granules also in myelomalacia, subacute combined degeneration of the cord, dementia paralytica, tumor of the brain (meningioma, carcinoma, astrocytoma) and Friedreich's ataxia, and in a case of severe herpetic encephalitis, but we failed to demonstrate them in case of suicide (by hanging). In the tumors of the brain studied, the silver granules and cells were analogous to those we described in other conditions, and in carcinoma of the brain they were present in immense masses, in even larger numbers than in any other condition, not excluding multiple sclerosis and dementia paralytica. In cerebral hemorrhage they were abundantly present in the adventitia of

the hyperemic blood vessels, near these vessels and also in the cerebral meninges. The granules were minute, of equal size and black and were in marked contrast to the pale yellowish homogeneous cores they surrounded, some of which were small and others large. When kept for twenty-four hours in a mixture of ether and dehydrated alcohol, the granules of the parenchyma disappeared, in contrast to what was observed by Steiner, though in the subarachnoid spaces and ganglion cells they appeared only less striking. Finally, the ganglion cells themselves

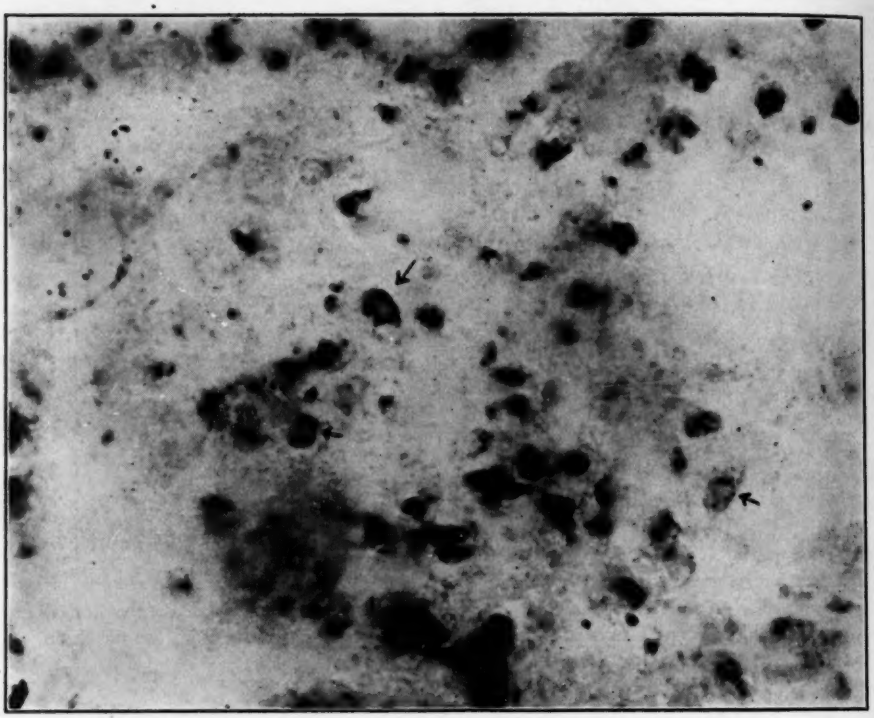


Fig. 4.—Subacute combined degeneration of the cord. Silver cells are indicated by arrows. The same cells are reproduced by hand in figure 2 *B*.

—in the spinal cord in multiple sclerosis and subacute combined degeneration of the cord—exhibited large accumulations of silver granules outside the nucleus and occupied the larger portion of the cytoplasm.

COMMENT

Of the areas that harbored silver granules, those around the axons, between the latter and the myelin sheath, were the most striking. Granules were absent in the patches of sclerosis because of the absence in them of nerve fibers which had become replaced by glial tissue; their

accumulation in large numbers in the transitional areas was due to the presence in the latter of numerous nerve fibers in the process of degeneration, which had not as yet been transformed into scar tissue; their rarity in the areas apparently normal could be explained by scarcity of degenerated fibers among them. The presence of silver granules in subacute combined degeneration of the cord, Friedreich's ataxia, myelomalacia, dementia paralytica and subacute bacterial endocarditis could also be ascribed to the presence of degenerated nerve fibers in these morbid conditions. The same is true of encephalitis, in which occasional single degenerated fibers can be demonstrated and in which the infiltrating hematogenous cells are mixed with gitter cells in the adventitial spaces.[14] The presence of granules in the amyloid bodies, always in large numbers, would also indicate a degenerative factor in their causation, for amyloid bodies are considered to be catabolic products and usually exist in degenerative neural lesions. The presence of granules in the adventitial, endothelial and white blood cells merely indicates that these cells probably contain argyrophilic substances which landed there from the degenerated parenchyma. Large numbers of silver cells and granules in carcinoma of the brain also can be explained by the presence of excessive amounts of degenerative products in such cerebral lesions. Their presence in the adventitial spaces of Virchow and Robin, the meninges or the subarachnoid space is somewhat difficult to explain. The silver cells are often near but not within the adventitial space, and it is possible that a degenerated nerve fiber harboring the granules becomes, as is the case with gitter cells, enveloped by the hyperplastic adventitia, as discussed elsewhere.[15] Whether such an explanation holds good for the presence of silver granules or silver cells in the cerebral meninges we are unable to tell. Histiocytes also may become impregnated with silver granules and carried through the tissue spaces to the adventitial spaces and from there, like any other pathologic material, to the subarachnoid space of the brain or spinal cord.

Steiner's silver-staining method generally permits one to demonstrate the presence of argyrophilic substance in various elements of the central nervous system, especially around the axon (figs 2 *B* and 4). No other silver-staining method brings out such silver granules, and in this fact lies, in our opinion, the value of Steiner's work. A relationship does exist between the threadlike or corkscrew-like formations resembeing spirochetes and the silver granules, but not in the sense Steiner suggested. The granules are not broken up spirochetes; they may only resemble them, especially in longitudinal sections of the nerve fibers, in

14. Hassin, G. B., and Bassoe, P.: A Contribution to the Histopathology of Epidemic ("Lethargic") Encephalitis, Arch. Neurol. & Psychiat. **2**:24 (July) 1919.

15. Hassin, G. B., and Bassoe, P.: Myelitis and Myelomalacia, Arch. Neurol. & Psychiat. **6**:32 (July) 1921.

which they are arranged in the form of chains. The granules thus do not cause the histologic changes seen in multiple sclerosis, but are the consequence of the latter, while Steiner claimed the reverse, that the spirochetes he described and represented by silver cells produce the histologic changes. He postulated that multiple sclerosis is "unquestionably" an infectious disease process analogous to disseminated encephalomyelitis, though he did not claim that the foci seen in these two morbid conditions are similar; that multiple sclerosis may run an acute or chronic course, and, accordingly, there may be acute, chronic and small (mostly perivascular) plaques, which by coalescing form larger ones; that the perivascular spaces are infiltrated with lymphocytes, plasma cells and "silver cells" or, what is the same, spirochetes; that the latter and other "noxa" invade the brain tissues from the subarachnoid space and cerebral ventricles by way of the perivascular spaces of Virchow and Robin.

It is needless to state that the pathologic features of multiple sclerosis can be given a different and probably a more plausible interpretation—that multiple sclerosis is not an inflammatory or infectious, but a degenerative toxic, disease process, and for this reason the plaques or patches, representing as they do the final stage of neural degeneration involving practically every nerve fiber in the central nervous system, are never young or acute; that in every case of multiple sclerosis, whether "young" or old, there are always fresh and old signs of neural degeneration, the fresh being represented by swelling and subsequent breaking up of the myelin followed by that of the axons; that the location of the plaques need not be perivascular, for the vascular supply has nothing to do with the formation and development of plaques.

As to the landing of spirochetes from the subarachnoid space in the perivascular spaces of Virchow and Robin, it would be proper to assume the reverse—that the spirochetes land in the cerebral parenchyma first, whence they invade the subarachnoid space, as the discharge of the contents of Virchow-Robin spaces is toward the subarachnoid space and not from it.[16] Noxious substances may enter the brain substance from the ventricles, but this occurs only under pathologic conditions, as is the case, for instance, in hydrocephalus[17]; under ordinary conditions the discharge is from the parenchyma into the ventricles; disseminated

16. Weed, L. H.: Studies on the Cerebro-Spinal Fluid, J. M. Research **31**: 21 (Sept.) 1914; An Anatomical Consideration of the Cerebro-Spinal Fluid, Anat. Rec. **12**:461, 1917. Hassin, G. B.: Effect of Organic Brain and Spinal Cord Changes on the Subarachnoid Space, Choroid Plexus and Cerebrospinal Fluid, Arch. Neurol. & Psychiat. **14**:468 (Oct.) 1925; Notes on the Nature and Origin of the Cerebrospinal Fluid, J. Nerv. & Ment. Dis. **59**:113, 1924.

17. Hassin, G. B.: Hydrocephalus: Studies of the Pathology and Pathogenesis, with Remarks on the Cerebrospinal Fluid, Arch. Neurol. & Psychiat. **24**: 1164 (Dec.) 1930; Hydrocephalus: Report of a Case in an Infant with Vestiges of a Choroid Plexus in the Fourth Ventricle Only, ibid. **27**:406 (Feb.) 1932.

encephalomyelitis[18] is clinically and pathologically a specific morbid entity and has nothing to do with multiple sclerosis, closely as the patches may resemble one another; the contents of the perivascular spaces of Virchow and Robin may be lymphocytes and plasma cells, but the main type of cell is the gitter cell, which lands there from the parenchyma.

On the whole, the pathologic features of multiple sclerosis are preeminently degenerative;[19] there may be superimposed on them inflammatory manifestations (lymphocytic and plasma cell infiltrations) which are considered secondary. A spirochetal infection does not cause such universal degenerations as are seen in multiple sclerosis, which are not observed even in dementia paralytica, which may resemble multiple sclerosis more than any other disease in some gross features. Phenomena of spirochetal invasion of the central nervous system, seen in dementia paralytica—pronounced leptomeningitis, granular ependymitis, preferable involvement of the ganglion cells and extensive inflammatory infiltrations of the Virchow-Robin spaces—would, at least partially, be present in multiple sclerosis were the latter due to a spirochetal infection. On the other hand, the patches of sclerosis which are typical of and numerous in multiple sclerosis are not common in dementia paralytica, in which they are exceptionally rare in the spinal cord. In fact, the only case in which patches (only three) of multiple sclerosis have been described in dementia paralytica was that of Spielmeyer.[20] Furthermore, the spirochetal theory of multiple sclerosis cannot explain the gradual and practically universal degeneration of the central nerve fibers, as this would suggest that spirochetes or silver cells are ubiquitous in the parenchyma, which is not the case. Nor is it to be assumed that the granules of "silver cells" in multiple sclerosis are old short-lived spirochetes, for then similar silver cells in dementia paralytica also should be considered products of short-lived spirochetes, which in dementia paralytica is by no means the case. Finally, the mere fact that spirochete-like formations similar to those seen in multiple sclerosis and silver granules are, as we have shown, also present in subacute combined degeneration of the cord

18. Hassin, G. B.: Disseminated Encephalomyelitis (Meningoencephalomyeloradiculitis) Versus Multiple Sclerosis, Arch. Neurol. & Psychiat. **40**:1111 (Dec.) 1938.

19. Hassin, G. B.: Studies in the Pathogenesis of Multiple Sclerosis, Arch. Neurol. & Psychiat. **7**:589 (May) 1922; Neuroptic Myelitis Versus Multiple Sclerosis, ibid. **37**:1083 (May) 1937; Pathologic Features of Multiple Sclerosis and Allied Conditions, ibid. **38**:713 (Oct.) 1937.

20. Spielmeyer, W.: Ueber einige anatomische Aehnlichkeiten zwischen progressiver Paralyse und multipler Sklerose (Untersuchungen über herdförmigen Markfaserschwund bei Paralyse), Ztschr. f. d. ges. Neurol. u. Psychiat. **1**: 660, 1910.

(figs. 1 and 4), myelomalacia, Friedreich's ataxia and even encephalitis and tumor of the brain would speak against spirochetes being their cause, for no one would claim that the aforementioned diseases are caused by spirochetes.

The few facts mentioned speak against the spirochetal nature of silver cells and force one to look for a different explanation of the presence of silver granules in multiple sclerosis and other conditions. Their presence can be explained by assuming that some catabolic process is instrumental in their formation, that they are what Alzheimer called "Abbau," probably in the nature of lipoids. Their dissolution in alcohol and ether would speak in favor of such a view. Their presence confirms the view that in multiple sclerosis there is a widespread degenerative lesion of the nerve fibers, preceded by swelling and breaking up of the myelin and followed by transformation of both into lipoids; these are stored within fat granule cells and removed from the tissue spaces to the Virchow-Robin spaces and thence to the subarachnoid spaces of the brain and spinal cord. In those areas in which the nerve tissue perished and became replaced by glial tissue, no granules or cells can be present, for the degeneration here is an accomplished process. In the areas in which the degeneration is, as it were, in full swing—the adjacent or transitional, superimposed areas—granules are exceptionally numerous, while in apparently normal areas they are rare, as here the myelin is merely swollen and not yet broken up. While Steiner's views as to the significance of the silver granules or cells discovered by him may need revision, the importance of his discovery cannot be overestimated, for it is possible to prove by his method the presence of an additional, new catabolic product indicating an early stage of degeneration of the central nervous system. So far it has not been possible to determine the chemical nature of the granules originating between the axon and the myelin. As has been stated, they are most likely lipoids. At any rate, they are not artefacts due to the various procedures used in their staining as in a normal brain studied by the same method the granules were not seen. Probably they are largely microscopic sediments of a substance holding the axon and myelin together, the first to undergo changes in degenerative pathologic conditions of the central nervous system.

CONCLUSIONS

1. "Silver cells" should be spoken of as "silver granules," for silver cells are probably not definite formations.

2. Silver granules are prominent not only in multiple sclerosis but in subacute combined degeneration of the cord, Friedreich's ataxia, myelomalacia, cerebral carcinoma and other conditions in which degeneration is an essential pathologic feature.

3. The granules are situated mainly between the axon and the myelin; they are probably lipoids and denote a metabolic disturbance of the central nervous system—an early stage of neural degeneration.

4. The granules are not artefacts, nor do they originate from spirochetes, but when arranged in chains they may assume a corkscrew spirochete-like appearance.

5. Such spirochete-like formations mixed with silver granules are seen in subacute combined degeneration of the cord, multiple sclerosis, myelomalacia and other degenerative or inflammatory-degenerative conditions.

6. The silver granules are present mainly in areas of extensive breaking up of the myelin, and their presence in multiple sclerosis confirms the view that this disease is one of degeneration and not of inflammation.

7. Steiner's method is a valuable aid in demonstrating early stages of degeneration of the central nervous system.

QUANTITATIVE ABSORPTION OF PHENOLSULFONPHTHALEIN FROM SUBARACHNOID SPACE

W. JAMES GARDNER, M.D.
AND
WILLIAM A. NOSIK, M.D.
CLEVELAND

In the study of normal and abnormal physiology of the nervous system it would be of considerable assistance to the clinician to know the quantitative return of the cerebrospinal fluid into the blood stream per unit of time.

It has long been known that certain substances when injected subarachnoidally eventually appear in the urine. In their study of such agents, the quantitative output of which from the subarachnoid space could easily be determined in the urine, Dandy and Blackfan [1] adopted neutral phenolsulfonphthalein for clinical use. After experimental trials it was concluded by these investigators that the quantitative results of the absorption of this dye from the human subarachnoid space are similar to those in animals; that is, for approximately three to four hours the absorption is fairly constant and then diminishes progressively as dilution with fresh fluid occurs. The dye appears in the urine in from six to eight minutes, while 35 to 60 per cent of the material is excreted in two hours. This normal standard of subarachnoid absorption of phenolsulfonphthalein was determined in patients in whom diagnostic lumbar puncture was done and apparently proved to be of considerable diagnostic value in the differentiation of obstructive from nonobstructive hydrocephalus in the infant.

Because of its importance, particularly in cases in which diminished subarachnoid absorption may be the factor responsible for the clinical picture, further investigations were made by Mehrtens and West [2] on the time at which this dye appears in the urine in both normal and pathologic states of the central nervous system. These authors noted that the dye appears in the urine of normal persons in ten minutes or less after subarachnoid injection and that the time of appearance is delayed by disease of the central nervous system, particularly of the

---

From the Cleveland Clinic Hospital.

1. Dandy, W. E., and Blackfan, K. D.: An Experimental and Clinical Study of Internal Hydrocephalus, J. A. M. A. **61**:2216-2217 (Dec. 20) 1913.

2. Mehrtens, H. G., and West, H. F.: The Absorption of Phenolsulphonephthalein from the Subarachnoid Space in Diseases of the Central Nervous System, Arch. Int. Med. **20**:575-585 (Oct.) 1917.

meninges, a fact which could not be accounted for by concomitant renal disease or reduction of the phenolsulfonphthalein in the cerebrospinal fluid. Quantitative estimations of the return of the dye were not presented, as the authors expressed the belief that the variations in its excretion were too great to be of value.

Weston [3] made similar qualitative studies on the time of appearance of this material in the urine of patients with dementia paralytica and dementia praecox. He concluded that the age, the duration of the psychosis and the physical and mental condition, as well as could be determined, had no constant effect on the time of appearance and that in all cases the dye was longer in making its appearance than the time for normal persons reported by Dandy and Blackfan (six minutes) and by Mehrtens and West (four to ten minutes). The time was found to vary from twelve to sixty-eight minutes for patients with dementia paralytica and from twenty-five to one hundred and four minutes for schizophrenic patients. Again, quantitative estimations of the amount of dye eliminated were not made.

It was for the purpose of determining the variability of the quantitative return of phenolsulfonphthalein in the urine after subarachnoid injection that this study was made.

The technic consisted essentially of making a lumbar puncture, injecting 1 cc. of neutral phenolsulfonphthalein after taking several cubic centimeters of fluid for examination and obtaining specimens of urine at the end of one and two hours from the time of injection.

TECHNIC

The procedure was as follows: The patient was instructed to empty his bladder immediately before the test, the specimen being discarded. With the patient on his side and the buttocks and shoulders at the same level, the skin was anesthetized with procaine hydrochloride. Lumbar puncture was made between the third and the fourth vertebra and a three way stopcock connected to the needle. Studies of pressure were made to insure patency of the canal, and 5 cc. of cerebrospinal fluid was taken, to be examined for cells, globulin and total protein and the Wassermann and the colloidal gold reaction. The secondary pressure was recorded, and a 5 cc. syringe containing 1 cc. of sterile neutral phenolsulfonphthalein was attached to the stopcock. The fluid was allowed slowly to fill the syringe until an even mixture of dye and fluid was obtained. This was then slowly injected. The mixture of fluid and dye was then again allowed to fill the syringe twice and was reinjected, assuring an even, diffuse dilution in the subarachnoid space. The patient's back had been straightened to minimize the back flow by altering the planes of tissue. Exactly one hour later the first specimen was taken, usually by catheterization, the patient having been instructed to drink at least two glasses of water in the interim. The procedure was repeated and a second specimen taken in another hour. Both specimens were then examined in the usual manner.

3. Weston, P. G.: Phenolsulphonephthalein Absorption from the Subarachnoid Space in Paresis and Dementia Praecox, Arch. Neurol. & Psychiat. **5**:58-63 (Jan.) 1921.

DATA

Of the patients thus examined, 16 showed no objective evidence of neurologic disease on either physical or laboratory examination. The requisites for membership in this group also included freedom from renal disease and cardiovascular involvement of such degree as might conceivably interfere with the test.

Included also are the records of 4 patients with syphilis of the central nervous system who underwent this examination and 4 with miscellaneous disease.

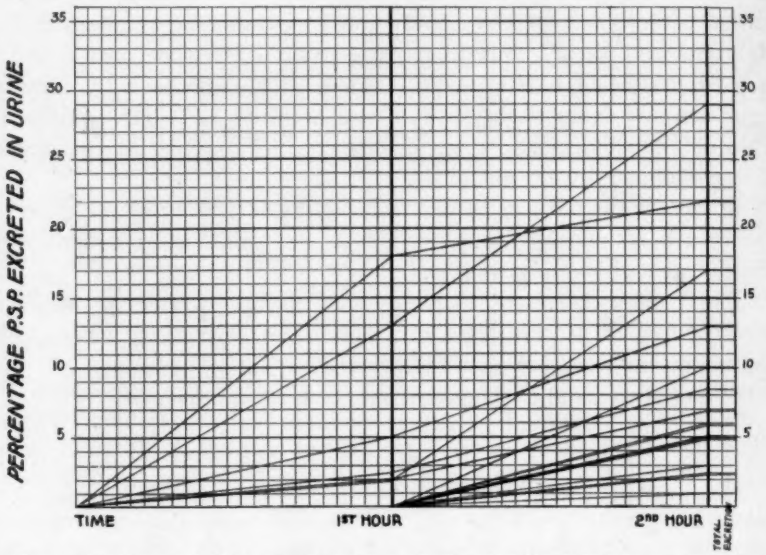


Chart showing variability in the return of phenolsulfonphthalein among normal subjects after one and after two hours.

The findings are charted in tables 1, 2 and 3; the chart shows the variability of the return after one hour and after two hours among normal subjects.

COMMENT

From the data presented it is obvious that however useful the quantitative intraspinal phenolsulfonphthalein absorption test might prove to be in a consideration of intracranial physiologic and pathologic conditions, the variations in its results in nonpathologic states are so great as to nullify its importance. There was no consistent decrease in the recovery of the dye among patients with syphilis of the central nervous system, as might be anticipated from the altered time of appearance observed by other authors, the variation being as great as it was in normal subjects. While the reduction of the dye in the spinal

TABLE 1.—*Data on Persons with no Physical or Laboratory Evidence of Organic Disease of the Central Nervous System*

No.	Age	Negated Impression	Wassermann Reaction: Blood	Wassermann Reaction: Cerebro-Spinal Fluid	Analysis of Spinal Fluid: Final Pressure, Mm.	Analysis of Spinal Fluid: Cells	Analysis of Spinal Fluid: Pandy Reaction	Analysis of Spinal Fluid: Total Protein, Mg.	Colloidal Gold Reaction	Quantitative Return of Phenolsulfonphthalein, %: 1st Hr.	2d Hr.	Total
1	55	Chronic cholecystitis	—	—	80	0	0	35	0000000000	0	5	5
2	20	Psychosis	—	—	110	0	0	35	0000000000	2	15	17
3	28	Multiple sclerosis (?)	—	—	80	0	0	30	0000000000	2	5	7
4	31	No abnormalities	—	—	70	0	0	30	0000000000	0	5	5
5	64	Neurosis	—	—	160	0	0	45	0000000000	0	3	3
6	39	Neurosis	—	—	40	0	0	55	0000000000	0	5	5
7	21	Mild trauma to head (later encephalogram normal)	—	—	120	0	0	35	0000000000	0	10	10
8	34	Neurosis	—	—	80	0	0	30	0000000000	5	8	13
9	45	Cervical periarthritis	—	—	140	0	0	30	0000000000	0	2½	2½
10	60	Petit mal, irritable colon	—	—	130	0	0	25	0000000000	0	6	6
11	60	Petit mal	—	—	130	0	0	25	0000000000	0	6	6
12	36	Cervical arthritis	—	—	80	0	0	20	0000000000	13	17	30
13	40	Functional disorder	—	—	50	0	0	*	0000000000	0	2½	2½
14	70	Silicosis	—	—	40	1	0	30	0000000000	2½	6	8½
15	41	Subdural effusion (?)	—	—	50	2	0	35	0000000000	18	5	23
16	44	Multiple sclerosis (?)	—	—	140	0	0	35	0000000000	0	1	1

* Quantity not sufficient for determination.

TABLE 2.—*Data on Persons with Syphilis of the Central Nervous System*

No.	Age	Wassermann Reaction: Blood	Wassermann Reaction: Cerebrospinal Fluid	Analysis of Spinal Fluid: Final Pressure, Mm.	Analysis of Spinal Fluid: Cells	Analysis of Spinal Fluid: Pandy Reaction	Analysis of Spinal Fluid: Total Protein, Mg.	Colloidal Gold Reaction	Quantitative Return of Phenolsulfonphthalein, %: 1st Hr.	2d Hr.	Total
1	47	+	+	150	23	Trace	60	3332100000	2½	2½	5
2	41	+	+	30	16	0	35	0000000000	5	15	20
3	31	+	+	120	9	Trace	40	1111110000	0	0	0
4	66	+	+	160	11	0	25	3332100000	0	0	0

TABLE 3.—*Data on Persons with Miscellaneous Diseases*

No.	Age	Diagnosis	Wassermann Reaction: Blood	Wassermann Reaction: Cerebrospinal Fluid	Analysis of Spinal Fluid: Final Pressure, Mm.	Analysis of Spinal Fluid: Cells	Analysis of Spinal Fluid: Pandy Reaction	Analysis of Spinal Fluid: Total Protein, Mg.	Colloidal Gold Reaction	Quantitative Return of Phenolsulfonphthalein, %: 1st Hr.	2d Hr.	Total
1	32	Multiple sclerosis	—	—	60	107	+	55	5555543100	10	5	15
2	34	Recovered spontaneous subarachnoid hemorrhage	—	—	150	Numerous	+	..	.....	10	20	30
3	40	Intramedullary tumor of cord	—	—	Block 50	4	+	100	0000000000	25	25	50
4	39	Parasagittal meningioma	—	—	160	0	+	45	0000000000	25	20	45

fluid was found by Mehrtens and West to range from 10 to 20 per cent in 18 different specimens of fluid for various periods, they expressed the belief that the slowness of absorption from the subarachnoid space, in addition to several unexplained features of the reductions, invalidates the quantitative but not the qualitative data on time of appearance in the urine. The work of Kendall [4] on the fate of phenolsulfonphthalein injected into the tissues indicated the changes which may occur before the final elimination and quantitative estimation of the dye. Great destruction of the dye results from an unnamed powerful reducing enzyme whose activity is enhanced by small amounts of dextrose, an increase in hydrogen ion concentration, slight acidosis, an increase in the concentration of the solution used, and reduction of the amount of oxygen in the tissue, which is necessary to protect phenolsulfonphthalein from destruction, together with changes in the composition and supply of blood and pulmonary conditions which tend to produce such a state. The extreme variations in the amount of dye recovered in our work may have been an expression of the influence of some of those factors. In the estimations of the degree of subarachnoid absorptive activity in cases in which delay in elimination of cerebrospinal fluid is suspected, it is our reaction that little assistance can be obtained from a quantitative study of the time of absorption of phenolsulfonphthalein, although qualitative determination of time of appearance may be of definite value.

CONCLUSION

Phenolsulfonphthalein injected into the subarachnoid space of normal persons appears in the urine in such varied percentages as to make the test of little value.

The quantitative return of the dye for normal persons was found to range from 1 to 30 per cent per two hour collection period.

In this series the recovery of the phenolsulfonphthalein for two hours was far below that previously reported as normal for the same time.

The quantitative estimation of phenolsulfonphthalein in testing for the degree of involvement of the cerebrospinal fluid absorption mechanism as determined by appearance-time studies is not reliable enough in the normal to place any credence on the findings in the altered state.

---

4. Kendall, E. C.: The Fate of Phenolsulphonephthalein When Injected into the Animal Organism, J. A. M. A. **68**:343-345 (Feb. 3) 1915.

RETURN OF COGNITIVE CONSCIOUS FUNCTIONS AFTER CONVULSIONS INDUCED WITH METRAZOL

LOUIS H. COHEN, M.D.
WORCESTER, MASS.

The present report is concerned with a systematic description and evaluation of the temporal order of return of the cognitive processes which "drop out" during the stuporous interval following convulsive seizures induced by metrazol in a group of schizophrenic patients. The functions which comprise the cognitive aspects of consciousness reappeared in the patients in an order which was so consistent that after some exploratory investigation it was possible to predict their occurrence accurately. Although the present data on the nature of disturbance of these functions and the order of their "normalization" may be specific for the postconvulsive period which characterizes metrazol-induced seizures, it is also possible that they may be more generally applicable to states of "clouded consciousness," "stuporousness" and "confusion" which characterize other postconvulsive clinical states. These clouded intervals are in need of more careful evaluation; except for the clinical descriptions of these states in terms of such concepts as orientation and memory, the literature contains no report of a systematic study of the nature of the return to normal consciousness. It is probable that the observations recorded here are not limited in their significance because of the nature of the patients' psychotic condition.

Immediately following the cessation of the grand mal seizure,[1] it was found that if the patient was pricked with a pin on any part of the body his response altered as time went on. At first no reaction could be observed. Shortly after this, however, the patient showed "mass reactions" to the prick; that is, no matter where he was stimulated he shifted his legs, arms or trunk into some other position, apparently in a random fashion. Following this, another phase was

From the Research Service of the Worcester State Hospital.

1. L. von Meduna (Die Konvulsionstherapie der Schizophrenie, Halle a. S., Carl Marhold, 1937), E. Friedman (The Irritative Treatment of Schizophrenia, Am. J. Psychiat. **94**:355-372, 1937; Irritative Therapy of Schizophrenia: Practical Application and Theoretical Consideration, New York State J. Med. **37**:1813-1821, 1937) and L. H. Cohen (Observations on the Convulsant Treatment of Schizophrenia with Metrazol, New England J. Med. **218**:1002-1007, 1938) have given detailed accounts of the nature of these convulsions.

observed which was characterized by a local defense reaction: If the arm or the leg, for example, was stimulated, the patient quickly withdrew that member. This period was succeeded in turn by one in which, in addition to the local defensive movements, the hand was brought to the region stimulated, which the patient would scratch. He did not usually scratch the actual point of stimulation (if he did so, it seemed by accident) but rather a wide area contiguous to it; for example, if he had been stimulated on the chest he might scratch over the abdomen and then the flank; if on the foot, then on the leg and thigh. Scratching was almost invariably in the vicinity of the point of stimulation, but not actually on it. This phase was followed by the interval, which persisted, in which the region of stimulation to the pinprick was exactly localized by the hand and in which warding-off movements were frequent. From even these rough clinical observations it seems that complete analgesia occurs during the earliest phase of the interval of unconsciousness and that as time goes on there occur intervals characterized first by inaccurate localization of the painful stimulus and eventually, but still early in the postconvulsive period, by the reestablishment of "normal" sensorimotor activity.

During the interval of inexact localization (dysesthesia) another interesting phenomenon was observed. If the patient was called by name it was clearly a matter of accident where he would turn his head to find whence he had been called; he might look to the right, to the left, up or down. Furthermore, if he were shown something, he appeared to look "through" the object rather than actually at it. It was during this period that his scratching movements were poorly localized. From such observations it is believed that during the interval of dysesthesia and for some time afterward—though in lesser degree—there was faulty ability to fixate and maintain attention (dysprosexia). This defect apparently grows out of the dysesthesia and then diminishes until finally the patient is again capable of attending adequately to the stimulation of touch, of sound and of sight.

With the gradual disappearance of the dysprosexia, another interesting feature of returning consciousness became evident. If one showed the patient some object, or if one placed some object in his hand and asked him what it was, he could not tell. A frank agnosia was thus demonstrated. A little later, and for some time after the dysprosexia had disappeared, one could observe what one might call dysgnosia; that is, the patient could identify some and later more and more objects until finally normal gnosia was again established.

However, even with normal gnosia it was observed that the patient did not make correct use of the objects. For example, if a key was handed to him he might answer that the object was a "key," but he

could not use it. In one instance this occurred while the patient was seeking to open a closed door; he was handed the key (which he called "key"), but instead of inserting it into the lock he played with it aimlessly or fumbled with it on the door or wall rather than inserting it into the lock. If told to put on his slippers he would pick up the correct object from the floor but might put his hand into it, put it on the wrong foot or, having finally put it on his foot, pull his socks on over it. Many observations of such dyspraxia were made. It was found that usually only after normal gnosia had been established for some time did the dyspraxia disappear.

In addition to the aforementioned disorders, there was observed another feature which various investigators of effects of metrazol have already noted, namely, amnesia. The amnesia persisted throughout all the aforementioned intervals and disappeared only after the various dysfunctions indicated had been normal for some time. The amnesia was both retrograde and anterograde. How the amnesia fits into the general schema is not clear; it is probably not independent of the functions described, but its connections with them could not be established from our observations.

The nature of the psychologic defects and the temporal order of their disappearance for patient E. T. are presented in the table. It indicates the clinical observations over an interval of about an hour following a grand mal seizure induced by metrazol.

COMMENT

One may consider the various functions described from the standpoint of their temporal relationship to each other. The order of their reestablishment seems to be: (1) esthesia, (2) prosexia, (3) gnosia, (4) praxia and (5) mnesia. To fit the return of memory into the schema has already been stated to be difficult at present, and will not be attempted. However, one may see that the ability to perform the proper act with an object (praxia) is greatly handicapped unless the ability to know what it is (gnosia) is present; and that this in turn is impossible unless the attention can be fixed selectively on it (prosexia), which in turn depends on sensitivity to external stimulation (esthesia).

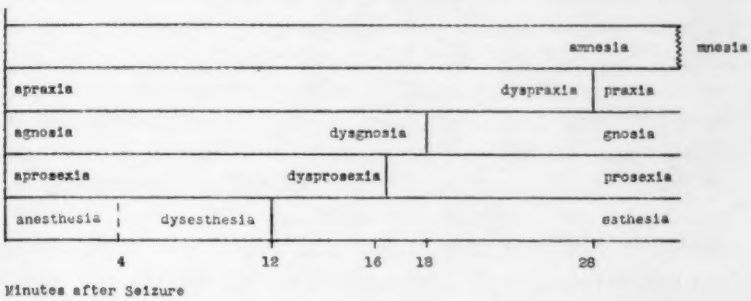
Although the duration of each "phase" has been found to be variable for different patients, the temporal order of reappearance of the functions studied has been found to be the same. The figure illustrates the status and the temporal order of reappearance of the cognitive processes studied here. For purposes of clarity the time intervals recorded for patient E. T. (table) are employed.

Nature and Temporal Order of Return of Cognitive Conscious Functions Following Convulsive Seizure for Patient E. T.

Time, P.M.	Minutes After Injection	Clinical Observations
2:12	0	Typical grand mal seizure
2:14	2	End of fit; patient deeply stuporous
2:15½	3½	Pinprick stimulation to: Midline of abdomen, left shoulder, right shoulder, midforehead, left leg, right leg, left flank, right flank, penis } no observed response
2:16	4	Pinprick stimulation to: Left leg: generalized movement of trunk, arms and legs Right leg: no observed response Right flank: grinding movement of jaw Left flank: generalized movements of legs Left shoulder, right shoulder: no observed response Patient called by name from left: no observed response
2:17½	5½	Patient relinquished mouth gag spontaneously Pinprick stimulation to: Right leg: withdrew right leg Left arm: withdrew left arm Midline of abdomen: no observed response
2:18	6	Pinprick stimulation to: Midline of abdomen: scratched widely over left flank with right hand Patient called by name from left: turned head to right Loud noise made behind head: no observed response
2:18½	6½	Pinprick stimulation to: Left leg: withdrew left leg and scratched diffusely over it and left thigh and back Midline of abdomen: scratched widely over left side with right hand Left flank: scratched diffusely over left flank; said, "Ow" Right flank: scratched diffusely over right flank; said, "Ow"
2:20	8	Pinprick stimulation to: Left leg: shouted, "Jiminy Christmas!"; scratched upper part of left thigh with right hand Midforehead: scratched over top of head with both hands Left flank: scratched widely over left flank with right hand Patient shown keys, asked "What's this?": looked "through" object Patient shown pencil, asked "What's this?": looked about in fashion suggestive of "seeking"
2:22	10	Pinprick stimulation to: Right leg: shouted "Hey!"; withdrew right leg, rubbed it with right hand Left flank: rubbed region of stimulation with right hand
2:24	12	Pinprick stimulation to: Midforehead: shouted. "Ow!"; no manual response Midforehead (repeated): brought right hand quickly to point stimulated Midline of abdomen: brought right hand quickly to point stimulated
2:25	13	Pinprick stimulation to: Left flank: rubbed diffusely over left side with right hand Right leg, Left leg, Right shoulder } withdrew limb quickly; brought hand to point stimulated and rubbed it Right shoulder (repeated): attempted to ward off pin although it was outside his field of vision Patient called by name from left: looked to left correctly Patient called by name from right: looked to right correctly Patient shown keys, asked "What's this?": looked at them briefly; did not answer Keys placed in patient's hand: played with keys awkwardly
2:27	15	Patient shown keys, asked "What's this?": looked fixedly at them, did not answer Patient asked "What's your name?": "E— T—" (correct) Patient asked "Where are you?": looked bewildered, did not answer
2:28	16	Patient shown keys, asked "What's this?": looked fixedly, did not answer Keys placed in patient's hand: played awkwardly with them Patient asked "What's your name?": "E— T—" (correct) Asked "Did I ask you that before?": answered "No" Patient shown pencil, asked "What's this?" } looked intently but Patient shown mouth gag, asked "What's this?" } did not answer Pencil, then mouth gag placed in patient's hand: played awkwardly with them
2:30	18	Patient shown keys, pencil, mouth gag, asked "What's this?": answered correctly Keys placed in patient's hand, asked "What do you do with this?"; answered "Open door" Patient helped out of bed and commanded "Open the door!": went to door, played with key against crack in door, then fumbled over right pane (lock on left panel)

Nature and Temporal Order of Return of Cognitive Conscious Functions Following Convulsive Seizure for Patient E. T.—Continued

Time, P.M.	Minutes After Injection	Clinical Observations
2:36	24	Patient handed a right shoe, asked "What's this?": answered "Shoe"; asked "What do you do with it?": answered "Wear it"; commanded "Put it on!": put it on left foot, stopped and stared at other shoe on floor beside him; commanded "Put on the other shoe!": began to roam around room, apparently looking for it, looked into corners and onto bed, passing over it on floor near him several times, finally put it on wrong foot after playing with it for a few moments; patient handed his socks: put socks on over the shoes, then picked up a towel and began to "put it on" as if getting into trousers, persevering in this for two minutes
2:40	28	Towel taken away from patient and trousers handed to him; put these on correctly, then reached down, removed his socks and shoes and put them on correctly, said "What's the matter with me, I must be going out of my mind," then, catching sight of the examiner making notes, said irritably "For God's sake, don't put that down!" then said "Where's my coat?"; handed bathrobe, asked "What's this?": "Bathrobe": "Are you sure?"; "Yes"; "Did you ask for your coat?"; "No." Patient put bathrobe on correctly, stumbled about awkwardly while doing so, but buttoned and tied bathrobe skilfully
2:44	32	Patient given his lunch: immediately began to eat, looked at examiner sheepishly, said "You're hot stuff, aren't you?" and smiled; asked, "Did you have an injection today?": answered, "No"; "Yesterday?": "Yes" (incorrect)
2:47	35	Patient said spontaneously "Of course I had an injection today in my right arm (correct), and you gave it to me"; asked "Who was with me?": named nurses and attendants correctly Memory for various procedures cited previously was tested: found to be fairly good for some of them, but there was no recollection of the pinpricks then or subsequently



Temporal order of reappearance of cognitive conscious functions.

This schema is concerned, obviously, with only the "cognitive" aspects of consciousness. These are not the whole of consciousness, for there are other aspects, for example, the volitional and affective, which have not been dealt with.

However, these data on the manner of reappearance of the cognitive functions following the interruption of the stream of consciousness seem to offer some illumination of the problem of the nature of the near-conscious state. As described and evaluated here, it appears that with the return to "normal" consciousness there is associated the realization of psychologic capacities in a sequence which depends on previously realized capacities. Hence, from the standpoint of the cognitive functions at least, it may be justifiable to conclude that in states of normal consciousness there are "layers" of functions, the more complex of which depend on the less complex. More work is needed, of course, to extend and make more precise the rough clinical observations pre-

sented here. It would appear that metrazol offers a rather simple and safe experimental method for inducing unconscious episodes.[2]

SUMMARY

The return of the cognitive conscious functions in the period following convulsive seizures is reported. The studies were carried out on schizophrenic patients during metrazol therapy. It was found that the cognitive functions reappear in a characteristic temporal order, indicating the dependence of a given function on preceding ones. The functions of esthesia, prosexia, gnosia, praxia and mnesia reappear in the order given. It is suggested that these studies be extended, since they have bearing on the general problem of the nature of consciousness. Furthermore, it appears that metrazol offers a safe and convenient means for the study of the interruption and normalization of the stream of consciousness.

2. It is probable that doses which produce convulsions are not necessary, since interruption of the stream of consciousness is possible with subconvulsive doses.

LIGATION OF THE LEFT ANTERIOR CEREBRAL ARTERY

ITS HAZARDS AND MEANS OF AVOIDANCE OF ITS COMPLICATIONS

JAMES L. POPPEN, M.D.
BOSTON

It is fairly well known among neurosurgeons that ligation of the left anterior cerebral artery is hazardous and may be followed by disastrous results. Dandy [1] emphasized this fact and has described a rather striking clinical picture observed after ligation of this artery. He said: "If the left anterior cerebral artery is injured by any chance the patient can never regain consciousness." He had personal experience with 2 patients who lived two and three weeks, respectively, after the artery had been ligated 2.5 cm. distal to the genu corporis callosi. His deduction was that the center of consciousness is located in the left cerebral hemisphere, in the region supplied by the left anterior cerebral artery; in other words, along the mesial aspect of the left cerebral hemisphere, near the anterior portion of the corpus callosum.

That this striking clinical picture of a permanent state of unconsciousness may be produced by ligation of the left anterior cerebral artery is demonstrated in my own experience (case 1), in which the results were as described in the 2 cases of Dandy. The patient lived three weeks after the ligation and during that time was completely unconscious, even though there was no evidence of increased intracranial pressure and reflex movement could be elicited only by strong stimulation over the supraorbital nerve. The eyelids opened and closed normally, but the eyes showed no comprehension or notice of immediate surroundings.

REPORT OF CASES

CASE 1.—A woman aged 43 was admitted to the New England Deaconess Hospital on Jan. 8, 1936, complaining of frontal headache on the right side and of frequent generalized convulsions during the preceding six years. She had been able to carry out her household activities until the past two months, when, according to members of her family, she acted peculiarly at times.

Read at a meeting of the Harvey Cushing Society, Memphis, Tenn., April 28, 1938.

From the neurosurgical service of the Lahey Clinic and from the New England Baptist and the New England Deaconess Hospital.

1. Dandy, W. E.: The Brain, in Lewis, D.: Practice of Surgery, Hagerstown, Md., W. F. Prior Company, Inc., 1932, vol. 12, chap. 1, p. 51.

Physical Examination.—There were considerable tenderness over the right frontal region, marked mental obtundity and a delayed reaction time for all verbal stimuli. The patient was facetious but well oriented as to place and time. The right pupil was slightly larger than the left; both, however, reacted to light and in accommodation. The ocular fundi showed the margins of the disks well demarcated, optic cups present and the retinal vessels unchanged. The deep reflexes were slightly increased on the left as compared with the right. Neurologic examination otherwise gave results essentially within normal limits.

Operation.—A ventriculogram taken on January 10 showed displacement of the right anterior horn to the left and shifting to the left of the anterior portion of the third venrticle.

A frontal craniotomy on the right was performed on the same day. During the operation a large soft, infiltrating tumor involving the entire right frontal lobe was subtotally removed by extensive right frontal lobectomy. It was noted at the time of operation that the tumor extended through the anterior portion of the corpus callosum to the left frontal lobe. The right anterior cerebral artery had been ligated just distal to the anterior communicating artery, and the left anterior cerebral artery was ligated 1.5 cm. distal to the anterior communicating artery. No attempt was made to remove any portion of the tumor occupying the medial surface of the left frontal lobe. The blood pressure was low at the time of the ligation and remained at 80 mm. of mercury systolic for the following twelve hours, when it came back to normal limits, as did the pulse and the respiratory rate.

Course.—The patient lived for twenty days after the operation and was physically well, but she could not be aroused and never regained any semblance of consciousness. Her eyes blinked and opened normally but did not seem to comprehend or follow any moving object in her immediate surroundings. Spinal puncture showed no increase in the intracranial pressure. On the twentieth day there was a sudden rise in pulse rate, temperature and respiratory rate, death following within a few hours.

Autopsy.—A large pulmonary embolus was the direct cause of death. The right and left anterior cerebral arteries had been ligated at the level indicated at the time of operation. There was no gross evidence of edema of the anterior portion of the corpus callosum or of the contiguous tissue on the mesial surface of the left frontal lobe. The tumor (glioblastoma multiforme) could be seen extending through the anterior surface of the corpus callosum into the medial portion of the left frontal lobe for a distance of 3 cm. Microscopic sections of cortex selected from the left frontal region and from both the right and the left parietal and occipital regions showed no changes except of moderate edema and perivascular hemorrhage.

Since this case demonstrated that a permanent state of coma does follow ligation of the left anterior cerebral artery, considerable time was spent in conjecture as to whether this unfortunate complication could be avoided.

Certainly, if the left anterior cerebral artery could be ligated without fear of disastrous results the left frontal lobe could be much more readily and radically removed. Since the brain has a well formed anastomosis of blood vessels it seemed unusual that ligation of the

left anterior cerebral artery should be so dangerous. From an anatomic standpoint it appears reasonable that much may depend on the site of ligation. It is conceivable, at least, that a sufficient amount of blood may flow through the anterior communicating artery if the occlusion is proximal to this point. Furthermore, a previous experience had shown that injury to the left anterior cerebral artery is not always followed by loss of consciousness.

CASE 2.—A woman aged 49 was admitted to the New England Deaconess Hospital with a history and symptoms typical of a large meningioma of the olfactory groove. The tumor was completely extirpated in a two stage operation on Sept. 27, 1934. At the second stage, during removal of the tumor capsule, which was adherent to all contiguous structures, it became necessary to ligate the left anterior cerebral artery 2 cm. distal to the anterior communicating artery. The pulse rate, respiratory rate and blood pressure were normal throughout the operation, and the patient regained consciousness as soon as the effects of the anesthetic had subsided. Meningitis from wound infection developed, and the patient died six weeks postoperatively. She was conscious and well oriented until shortly before death. Autopsy revealed that the left anterior cerebral artery had been completely occluded by a silver clip 2 cm. distal to the anterior communicating artery.

Since I had been aware of the fact that the left anterior cerebral artery had been ligated in case 2, the patient was watched carefully for any changes in her state of consciousness. When she became fully conscious in the normal period after anesthesia, some skepticism arose as to whether ligation of the left anterior cerebral artery in the absence of other factors should cause the clinical picture previously described. When this condition did arise in case 1, both operative notes and records of the pulse rate, the respiratory rate and the blood pressure during the period of anesthesia were carefully studied. Since the anesthetist had been unaware that the artery had been ligated in either case, no notations were made on the anesthesia record as to the exact time of ligation. The only outstanding difference, however, in the operative course of the patients was that in case 1 the blood pressure was low at approximately the time when the artery had been occluded and remained so throughout the operation and for several hours afterward, whereas in case 2 the blood pressure had been within normal limits throughout the operative procedure, ranging from 120 to 140 mm. of mercury systolic.

In personal correspondence with Dr. J. F. Fulton, of Yale University, the problem was discussed because of his neurosurgical experience with the higher apes. He expressed the opinion that if the blood pressure remains within normal limits at the time of ligation the resulting localized anemia will not cause permanent damage, since adequate blood supply will be carried by the collateral circulation. On the other hand, if the blood pressure is low at the time of ligation the resulting anemia

will be sufficiently intense to cause diminution in the collateral circulation to such an extent that permanent cellular changes will take place.

That the state of consciousness following ligation of the left anterior cerebral artery or both anterior cerebral arteries depends to a great extent on the condition of the patient, especially on the blood pressure at the time of ligation, has been found to be true in subsequent cases in which it became necessary to occlude the artery.

Obviously, there are times when it is desirable to ligate the left anterior cerebral artery, especially in an extensive resection of the left frontal lobe. If the ligation can be done without serious consequences early in the operation, the entire procedure is much more readily accomplished. Great care must be exercised also in ligating the right anterior cerebral artery, because of its proximity to the left. It is necessary frequently to separate the two trunks in order to avoid including both arteries when the clip is intended for only one.

In the neurosurgical department of the Mayo Clinic ligation of the left anterior cerebral artery has been done in 10 patients since 1934. The sites of the ligations are shown in figures 1 and 2. In cases 1 and 2 no attempt was made to keep the patient's blood pressure within normal limits, since it was not known to be of any significance in relation to the ultimate state of consciousness if the artery was ligated. Since my experience with the first 2 patients it has always been my policy to keep the blood pressure well within normal limits when there is any possibility of injury to the left anterior cerebral artery. In the subsequent 8 cases it was necessary to occlude the artery in order that a satisfactory enucleation of a tumor might be accomplished. In 2 of the patients the blood pressure was low when the ligation was contemplated, and ligation was delayed until the blood pressure had been brought up to normal limits by intravenous infusion either of a stimulant or of whole blood.

In order that the blood pressure may be kept at approximately the normal level throughout the operative procedure, it is advisable to have a cannula inserted into a vein of the leg before the craniotomy is started. With such a preliminary measure, no confusion results during an unexpected sudden lowering of blood pressure. In this department it has been the practice for the past four years to insert a cannula for constant intravenous infusion in all cases of major craniotomy while the patient is being anesthetized. It has been noted that a more uniform course is run if 5 per cent dextrose in saline solution is given throughout the procedure. The flow of the infusion is regulated by the patient's condition. The measure has advantages also in avoiding all unnecessary delay in administering any intravenous medication that it is thought necessary to give.

To facilitate the introduction of the cannula a special stilet (fig. 3) has been devised. This eliminates the necessity of a vein spreader. The exposure of the great saphenous vein through a small opening in the

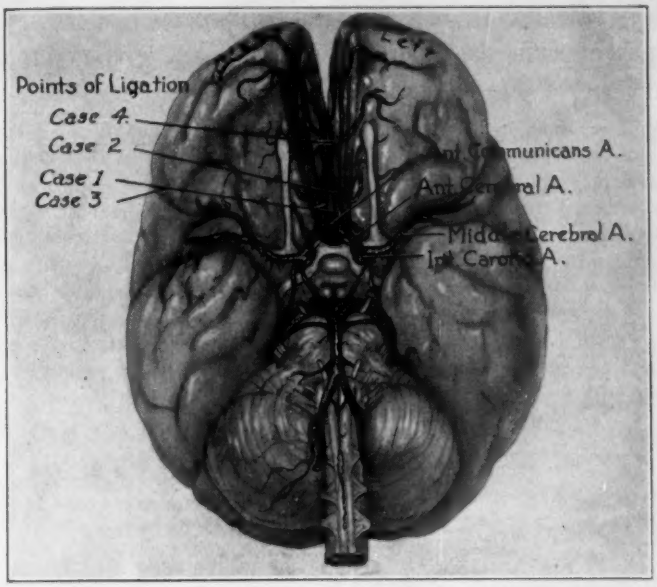


Fig. 1.—Sketch of the circle of Willis, indicating the site of ligation of the left anterior cerebral artery in the first 4 cases.

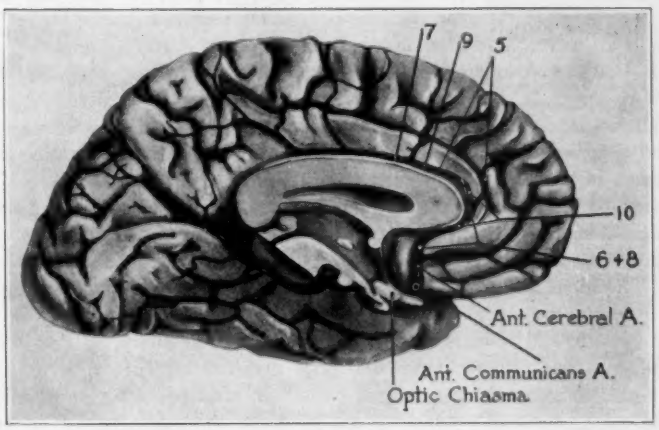


Fig. 2.—Site of ligation of the left anterior cerebral artery in cases 5 to 10.

skin just above and medial to the malleolus medialis can readily be accomplished by use of a small nerve hook. The cannula may be left in situ up to one week if necessary. The leg should be watched care-

fully, however, for signs of infection. If any local redness appears, the needle should be removed immediately and hot dressings applied.

As has been stated, I have had occasion to ligate the left anterior cerebral artery (in 2 instances both the right and the left) in 8 patients besides those whose cases have been described. It is believed that the subject is of sufficient importance to warrant a brief report of each of these additional cases.

CASE 3.—A man aged 50 entered the hospital on June 7, 1936, because of convulsions during the past six weeks. Since there was evidence of increased intracranial pressure with no localizing signs, ventriculograms were taken on June 8, after which a frontal craniotomy was performed on the left. A fibrillary astrocytoma was extirpated by wide resection of the entire left frontal lobe, during which ligation of the left anterior cerebral artery was carried out. In the placing of the clip on the left anterior cerebral artery the right was included unintentionally. The blood pressure was normal at the time of ligation and remained so. The patient regained a normal state of consciousness after recovery from the anesthesia, and after a convalescence of six weeks he has returned to his regular occupation, delivering milk from house to house.

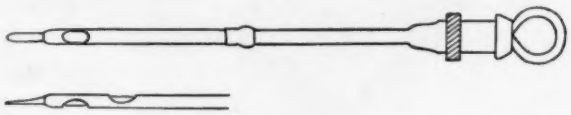


Fig. 3.—Ordinary cannula with special stilet used.

This case illustrates the point already made: Since the anterior cerebral arteries are so intimately situated, great care should always be taken in separating the main trunks so that both are not inadvertently included in one clip.

CASE 4.—A woman aged 50 was admitted to the New England Deaconess Hospital on Aug. 20, 1936. She complained of severe bifrontal headaches of one year's duration and of blurring vision for the past five months. Two weeks before her admission she began to have nausea, vomiting, urinary incontinence and a grave defect in memory. Ventriculograms taken on September 4 revealed evidence of a lesion of the left frontal lobe. Complete removal of the left frontal lobe, including a tumor (glioblastoma multiforme), was performed. It was necessary to ligate the left anterior cerebral artery 3 cm. distal to the anterior communicating artery. The blood pressure at the time of ligation was within normal limits and remained so for one hour. After this the blood pressure dropped to 90 mm. of mercury systolic and remained at this level for several hours, so that the patient had regained consciousness before the blood pressure returned to a normal level. She was able to carry out her normal household activities for nine months. This was followed by signs of recurrence and by death approximately ten months after the operation.

CASE 5.—A man aged 28 was admitted to the New England Deaconess Hospital on July 4, 1937, because of headaches and vomiting of ten days' duration. A

glioblastoma multiforme involving the left frontal lobe was extirpated by wide resection of the entire frontal lobe. The left anterior artery and a large anterior branch were clipped at the genu corporis callosi. The patient regained consciousness after the effects of the general anesthetic (avertin in amylene hydrate and ether) had subsided. At the time of this report, nine months later, he is carrying out his regular activities as a gardener, with no signs of recurrence.

The ligation in case 5 was performed deliberately, since the blood pressure was within normal limits at the time the artery was occluded.

CASE 6.—A woman aged 38 was admitted to the New England Deaconess Hospital on July 18, 1937, because of signs of increased intracranial pressure. On July 19 ventriculograms were taken and craniotomy was carried out. A large hemangioblastic meningioma of the anterior portion of the falx was removed completely. During the operation it became necessary to ligate the left anterior cerebral artery at two levels, 1 cm. distal to the anterior communicating artery and again at the genu corporis callosi. One-half hour after the ligation the blood pressure dropped suddenly to 80 mm. of mercury systolic. The patient was given a small blood transfusion, which caused a rise in blood pressure to 110 mm. systolic within fifteen minutes of the drop.

The patient regained consciousness in a normal period after the effects of the anesthetic had subsided. At the time of this report, after a convalescence of eight weeks, she is carrying out her duties as a stenographer.

CASE 7.—A woman aged 40 was admitted to the New England Deaconess Hospital on July 5, 1937, because of headaches and loss of weight for fifteen months and abnormal fatigability for one year. The headaches were usually occipital, were described as "bursting" and were so severe as to keep the patient in bed as long as three days at a time. They were associated with a slight degree of nausea and vomiting. She also had noticed a slight weakness of the right arm during the past month.

Neurologic examination revealed choking of the optic disks, with no other significant lcoalizing signs. Roentgenograms of the skull showed destruction of the sella turcica. The visual fields, however, were normal. On July 28 a large hemangioblastic meningioma of the falx, which completely replaced the right frontal lobe and part of the left, was removed totally. It became necessary to ligate the left anterior cerebral artery 3 cm. distal to the genu corporis callosi. The blood pressure remained normal during the procedure. The patient regained consciousness in a normal period after the effects of the general anesthetic (avertin with amylene hydrate and ether) had subsided. When last heard from, six months after her discharge from the hospital, she was carrying out her duties as a housewife.

CASE 8.—A man aged 60 was admitted to the New England Deaconess Hospital on Aug. 13, 1937, because of disturbance in concentration and memory for two weeks. The patient had worked until the day of his admission. Because of signs of increased intracranial pressure with indefinite localizing signs, ventriculograms were taken on August 19; they showed displacement of the anterior horn of the left lateral ventricle. On the same day a left frontal lobectomy, including all the tumor grossly discernible, was performed. The left anterior cerebral artery was ligated 1 cm. distal to the anterior communicating artery and at the genu corporis callosi. The blood pressure was within normal limits at the time of ligation. A normal state of consciousness followed recovery from the effects of the anesthetic.

The patient was discharged from the hospital two weeks after the craniotomy and was making a normal recovery when last heard from, six weeks later.

CASE 9.—A woman aged 52 was admitted to the New England Deaconess Hospital on Feb. 16, 1938, with a diagnosis of unlocalized tumor of the brain. She complained of headaches and of several convulsions during the past year. Ventriculograms were taken and craniotomy was done on February 18. A large meningioma of the left frontal lobe, which was attached to the inferior border of the anterior portion of the falx at the level of the genu corporis callosi, was removed. During the enucleation it became necessary to ligate the left anterior cerebral artery 3 cm. distal to the genu corporis callosi. The blood pressure was within normal limits at the time of ligation and remained so for three hours, when it started to fluctuate between 80 and 100 mm. of mercury systolic. Intravenous injection of dextrose and a small blood transfusion brought the pressure back to a normal level. The patient's state of consciousness was normal after her recovery from the effects of the anesthetic, but she had practically complete aphasia for two days after the operation. The aphasia rapidly disappeared, and recovery took place without untoward changes.

Case 9 demonstrates that the left anterior cerebral artery may be ligated posterior to the genu corporis callosi without changes in the state of consciousness if the proper precautions are taken. The postoperative aphasia was no more than that observed after a craniotomy on the left, in which considerable edema occurs owing to necessary manipulation of the brain during removal of the tumor.

CASE 10.—A woman aged 56 was admitted to the New England Deaconess Hospital on March 14, 1938, because of headaches, vomiting, decreasing vision and staggering gait since November 1937.

Neurologic examination revealed bilateral choking of the optic disks but very few localizing signs. Ventriculograms were taken on March 16, 1938. Marked displacement of the ventricular system to the right and depression of the left anterior horn were noted. An osteoplastic bone flap in the anterior part of the left central region was turned down. By separation of the venous attachments to the sagittal sinus the medial portion of the left frontal and the parietal lobe was greatly retracted laterally. The tumor was firmly attached to the lower margin of the falx and the anterior cerebral vessels as they came over the genu corporis callosi. In enucleation of the tumor it became necessary to ligate the main trunk of the anterior cerebral artery 3 cm. distal to the anterior communicating artery and again 2.5 cm. posterior to the genu of the corpus callosum. In this patient the systolic blood pressure was 80 mm. of mercury at the time ligation was thought necessary. The procedure was delayed until the pressure was brought up to normal limits by transfusion. Postoperatively the patient was aphasic and had considerable weakness of the right arm and leg; she remained in a semicomatose condition for three days. At the time of this report, two months after her discharge from the hospital, she is still somewhat aphasic but is conscious and able to carry on an intelligible conversation. Microscopically the tumor proved to be a metastatic adenocarcinoma.

Case 10 also demonstrates that the left anterior cerebral artery may be ligated posterior to the genu corporis callosi without serious interference with the state of consciousness. Particular precautions were

taken that the blood pressure should be normal at the time of ligation. The temporarily semicomatose condition of the patient was due mainly to postoperative edema.

SUMMARY

Ligation of the left anterior cerebral artery has been performed in 10 patients (bilaterally in 2).

Under certain conditions such ligation may be followed by permanent unconsciousness.

In my experience, if the blood pressure is kept within normal limits the ligation may be done without untoward changes in the state of consciousness.

Constant intravenous infusion of dextrose in saline solution is advocated in all cases of major craniotomy in which the left anterior cerebral artery may be injured. This may have to be supplemented with pressor substances or with whole blood.

ACTION OF METRAZOL (PENTAMETHYLENETETRAZOL) ON THE HYPOTHALAMUS OF THE CAT

JULES H. MASSERMAN, M.D.
WITH THE TECHNICAL ASSISTANCE OF E. W. HAERTIG
CHICAGO

It is my purpose in this report to present the results of a series of experiments designed to investigate the effect of pentamethylenetetrazol (metrazol), when injected either intravenously or directly into the diencephalon, on the functions of the hypothalamus and on its responses to faradic stimulation in anesthetized and in recovery preparations.

METHODS

The experimental methods employed in these studies have been described in detail elsewhere;[1] in brief, they were as follows:

Acute Preparations (8 animals).—A cat was placed under light ether anesthesia and was prepared for kymographic recording of the respiration and the blood pressure. An insulated bipolar needle electrode was then inserted into the hypothalamus by the Horsley-Clarke stereotaxic technic, rendering possible observations of the muscular and vegetative reactions to faradic stimulation of the hypothalamus and the changes in these reactions produced by the intravenous or intradiencephalic injection of a solution of metrazol.

Recovery Preparations (7 animals; 15 experiments).—With the animal under anesthesia induced with pentobarbital sodium, an insulated needle electrode was directed stereotaxically into the hypothalamus and fixed firmly to the cat's skull. After recovery from the operation the animal was observed in an active, unham-

From the Division of Psychiatry of the Department of Medicine, the University of Chicago Clinics, and the Otho S. A. Sprague Memorial Institute, the University of Chicago.

1. (*a*) Horsley, V., and Clarke, R. H.: The Structure and Functions of the Cerebellum Examined by a New Method, Brain **31**:45, 1908. (*b*) Clarke, R. H., and Henderson, E. E.: Investigations of the Central Nervous System: Methods and Instruments, Baltimore, Johns Hopkins Press, 1920. (*c*) Ranson, S. W.: On the Use of the Horsley-Clarke Stereotaxic Instrument, Psychiat. en neurol. bl. [**38**]:534, 1934. (*d*) Masserman, J. H.: Effects of Sodium Amytal and Other Drugs on the Reactivity of the Hypothalamus of the Cat, Arch. Neurol. & Psychiat. **37**:617 (March) 1937; (*e*) Destruction of the Hypothalamus in Cats: Effects on Activity of the Central Nervous System and Its Reaction to Sodium Amytal, ibid. **39**:1250 (June) 1938; (*f*) The Effects of Strychnine on the Emotional Mimetic Functions of the Hypothalamus of the Cat, J. Pharmacol. & Exper. Therap. **64**:335 (Nov.) 1938.

pered state for the effects of electrical stimulation of the hypothalamus before and after the intravenous or intradiencephalic injection of metrazol.

Anatomic Preparations.—The brain of each animal was stained in serial sections and examined microscopically to confirm the placement of the tip of the needle in the region selected for study: the right or the left half of the tuber cinereum, 2 to 3 mm. from the midline. The laterality of placement had no significant influence on the results observed in these experiments.

RESULTS

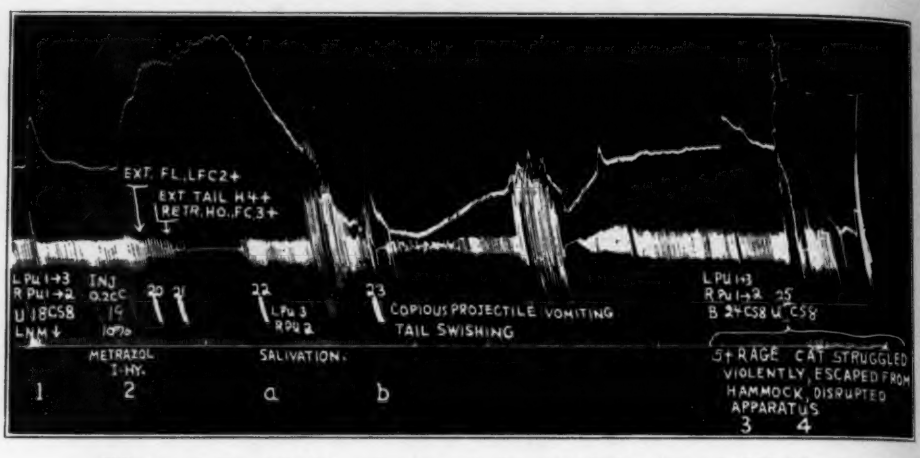
Recovery Preparations.—The intravenous injection of 1 cc. of a 10 per cent solution of metrazol caused no observable effects if the injection took longer than twenty seconds; however, if from 0.6 to 1 cc. of the solution was injected in from two to four seconds, the animal reacted in about ten seconds with tonic extensor spasms, opisthotonos and apnea lasting up to forty-five seconds. These effects were succeeded by hyperpnea, mydriasis, piloerection, retraction of the nictitating membranes, extrusion of the claws and clonic convulsions, gradually diminishing in intensity and severity over a period of from five to ten minutes.

Intradiencephalic Injections.—In control experiments previously reported,[1d] the injection of as much as 0.3 cc. of neutral Locke's solution through the needle electrode directly into the hypothalamus produced no observed effects if the injection was made at a rate of less than 0.1 cc. per minute. However, in the present experiments the slow injection of 0.05 cc. of a 10 per cent solution of metrazol produced a series of responses which were typically as follows: In from one to two minutes the animal began to vocalize in characteristically deep and agitated meows, which changed to growls and snarls if the animal was handled. A few seconds later the animal started to sneeze, salivate profusely, lick or bite its jaws, claw its head bandage and act in an increasingly restless, disturbed and then vicious manner. After about four minutes the animal, vocalizing loudly, with pupils dilated, claws extruded and hair erect, began to run about the laboratory, scrambling over furniture, attacking small objects or pushing with legs and body tensely braced against larger obstacles in its path. In some animals, retching, vomiting, urination and defecation also occurred. In general, the motor excitement, vegetative disturbances and emotional irritability reached a peak about ten minutes after the injection and then gradually subsided during the next fifteen minutes, the hyperpnea usually being the last effect to disappear.

Acute Preparations.—In cats under light ether anesthesia the slow intravenous injection of up to 1 cc. of a 10 per cent solution produced no obvious effects; however, when the solution was injected as rapidly as possible, tonic and clonic convulsions like those seen in the recovery animals appeared. In two experiments the blood pressure remained unchanged except for minor irregularities coincident with the convulsive movements, but in the other two it fell rapidly from 20 to 45 mm. of mercury before the convulsion and then returned to the base line or above during the seizure. Hypopnea after the injection was less marked in the anesthetized than in the survival animals, but the postconvulsive hyperpnea was equally intense in both series.

The injection of from 0.1 to 0.2 cc. of the solution of metrazol into the hypothalamus of an animal anesthetized with ether (figure) was followed within about a minute by variable cyclomotor effects, piloerection, salivation, urination, panting, blinking of the eyelids and nictitating membranes, champing and biting movements of the mouth, extrusion of the claws, lashing of the tail, torsion of the body.

swinging of the head and running or pawing movements of the legs, the last sometimes being dissociated in tempo and rhythm. During from the next three to five minutes these effects increased in intensity until in some instances the animal seemed to waken even from deep anesthesia (figure, *4*) and could only with difficulty be kept in the experimental hammock. The pseudoaffective reactions remained at maximal intensity for a minute or two and then gradually subsided during the following eight to twelve minutes.



Effects of the injection of metrazol (pentamethylenetetrazol–$C_6H_{10}N_4$) into the hypothalamus of a cat under ether anesthesia.

From above downward, the tracings represent the blood pressure, the respiration, the signal magnet record and the time, expressed in seconds. The following symbols are used: *B* indicates bipolar faradic stimulation, the numeral within the jog of the signal line representing the serial number of the stimulus in the experiment; *CS*, the setting of the secondary coil on the Harvard inductorium, expressed in centimeters; *Ext*, extension; *FC*, extrusion of the foreclaws; *H*, erection of hair; *Hd*, head; *I-Hy*, intrahypothalamic injection; *L*, left; *NM*, nictitating membrane; *Pu*, pupils; *R*, right; *Retr*, retraction, and *U*, unipolar faradic stimulation. The intensity of the reactions is rated on a scale of from 0 to 5.

At *1*, unipolar stimulation of the hypothalamus with a faradic current from the secondary coil of a Harvard inductorium (coil separation 8 cm., primary current 1.5 volts) as a control produced moderate mydriasis, a downward movement of the left nictitating membrane, a slight rise in blood pressure and an increase in the rate of respiration coincident with a decrease in its volume. At *2*, 0.2 cc. of a 10 per cent solution of metrazol was injected slowly into the hypothalamus, resulting first in hypopnea and apnea with vascular hypertension and then in hyperpnea accompanied by a fall in the blood pressure. At intervals after the injection, various muscular movements, mydriasis, salivation, unsheathing of the claws, marked piloerection, lashing of the tail and, finally, projectile vomiting occurred, as noted in the tracing. At *4*, repetition of the unipolar faradic stimulus caused a marked accentuation of all these effects (*5 + rage*) and pseudoaffective reactions of such intensity that the cat, partially waking from the anesthesia, struggled free from the hammock and terminated the experiment.

Effects on Blood Pressure and Respiration.—The blood pressure in anesthetized animals usually began to rise during or shortly after the intradiencephalic injection of metrazol and reached a maximum of from 20 to 70 mm. of mercury

Effect of Intradiencephalic Injections of Metrazol in Anesthetized Preparations on Hypothalamic Reactions to Faradic Stimulation *

	A Homolateral Stimulation After Injection				B Contralateral Stimulation After Injection			
	Stimulation: 2 Volts Unipolar $R_2A_{12}H_{-4}$ Injection: 0.2 Cc. 10% Metrazol $R_2A_{12}H_{-4}$		Stimulation: 4 Volts Bipolar $R_2A_{12}H_{-4}$ Injection: 0.2 Cc. 10% Metrazol $R_2A_{12}H_{-4}$		Stimulation: 1 Volt Unipolar $R_2A_{12}H_{-4}$ Injection: 0.1 Cc. 10% Metrazol $R_2A_{12}H_{-4}$		Stimulation: 6 Volts Bipolar $R_2A_{12}H_{-4}$ Injection: 0.1 Cc. 10% Metrazol $R_2A_{12}H_{-4}$	
	Before Injection	After Injection	Before Injection	After Injection	Before Injection	After Injection	Before Injection	After Injection
Pupils	4+	5+	3+	4+	3+	4+	3+	4+
Hair	0	4+	0	0	0	0	0	0
Claws	Left foreleg 2+	All claws 4+	0	Both forelegs 2+	0	0	Left foreleg 2+	All claws 2+
Nictitating membranes	2+	4+	2+	4+	0	2+	2+	3+
Legs	1+ Flexion of right hindleg	4+ Pawing and struggling	1+ Pawing of hindleg	Extension of forelegs 3+; pawing of hindlegs	0	Extensor tonus	1+ Pawing	3+ Pawing
Head	1+ Torsion to left	4+ Torsion to left	2+ Torsion to left	4+ Torsion to left	0	2+ Torsion to left	2+ Torsion to left	4+ Torsion to left
Urination	+	+	+	+	0	0	+	+
Blood pressure, mm. of mercury	+48	+82	+28	+70	+12	+46	+40	+66
Respiration								
Rate	+1	+2	+1	Apnea	0	Apnea	+2	Apnea
Depth	+1	+2	−1	Apnea	0	Apnea	+1	Apnea
Effects after stimulation	0	Strong struggling	Licking	Licking; biting; salivation	Licking	Strong jerk of head to left	0	Strong biting

* This table lists the average magnitudes of the various responses obtained in all experiments by faradic stimulation of the hypothalamus before and after the intradiencephalic injection of 0.2 cc. of a 10 per cent aqueous solution of metrazol (pentamethylenetetrazol). In part A, the stimuli and the metrazol are applied to the same point in the right side of the hypothalamus; as may be seen, nearly all the responses are markedly enhanced after the injection, especially on unipolar stimulation.

Part B shows the responses to stimulation of the right side of the hypothalamus before and after the injection of 0.1 cc. of a 10 per cent solution of metrazol into the left side of the hypothalamus. In these experiments, heightened excitability to both bipolar and unipolar stimulation appears also on the side opposite that of injection, but this is less consistent and less marked than after homolateral injection.

The sites of injection and stimulation are indicated by the Horsley-Clarke stereotaxic coordinates; e. g., $R_2A_{12}H_{-4}$ indicates that the tip of the needle electrode is 2 mm. to the right of the midline, 12 mm. anterior to the interaural coronal plane and 4 mm. below the zero horizontal plane.

All responses are roughly graded from minus 5 (maximal decrease) to plus 5 (maximal increase), zero indicating that no change from the prestimulation state was produced by the stimulus. Apnea may be regarded as a greater response than an increase or partial decrease in the respiratory movements.

above normal at about the time the first emotional mimetic responses appeared (figure, *2*). In two experiments the intravascular tension then rapidly returned to base line or below; in the others it remained elevated for from forty-five to ninety seconds before returning to normal. The degree of rise in blood pressure was roughly proportional to the quantity of metrazol injected, but no consistent changes in pulse pressure were observed.

About a minute after the injection of metrazol into the hypothalamus there occurred in 5 experiments marked hyperpnea which lasted for from two to twenty minutes. However, in 3 animals (figure) a period of apnea was induced, while in another deep respiratory gasps occurred every seven seconds for about ten minutes after the injection.

Electrical Stimulation after the Injection of Metrazol.—As previously reported,[1f] bipolar stimulation of the hypothalamus in a recovery preparation with a 60 cycle faradic current of from 2 to 6 volts caused salivation, mydriasis, piloerection, forced urination, extrusion of the claws, lashing of the tail and biting, clawing and fighting movements, followed after the cessation of the stimulus by the precipitate flight of the animal. In anesthetized animals these effects were accompanied by biphasic changes in the respirations and in the blood pressure (figure). The intravenous injection of up to 1 cc. of metrazol in either a survival or acute preparation produced no change in the responses to faradic stimulation of the hypothalamus, whether or not convulsions were produced by the injection. However, from 0.05 to 0.2 cc. of the solution injected into the diencephalon of an acute preparation caused marked lowering of threshold and an increase in the intensity of the responses to either unipolar or bipolar stimulation during a period of ten minutes following the injection (figure, *1* and *4*). This increased reactivity was more marked on the side of injection, but appeared, although less consistently, also on the contralateral portion of the hypothalamus (table).

COMMENT

Metrazol (pentamethylenetetrazol), long in use as an analeptic [2] and as an agent for the production of experimental convulsions,[3] has lately

2. (*a*) Eichler, O., and Hildebrandt, F.: The Action of Cardiazol on the Circulation, Arch. f. exper. Path. u. Pharmakol. **116**:100, 1926. (*b*) Voss, J.: The Action of Cardiazol Given by Mouth, ibid. **118**:259, 1926. (*c*) Franken, H.: Action of Caffeine, Cardiazol, Coramine and Ephetonine on Blood Pressure and Respiration, Klin. Wchnschr. **9**:1124, 1930. (*d*) Gremels, H.: Circulatory Action of Cardiazol, Coramine and Hexetone, Arch. f. exper. Path. u. Pharmakol. **153**: 36, 1930. (*e*) Goworow, N., and Speranskaja-Stepanowa, E.: Effect of Cardiazol on Blood Pressure, Ztschr. f. d. ges. exper. Med. **79**:517, 1931. (*f*) Maloney, A. H., and Tatum, A. L.: Cardiazol (Metrazol) and Coramine as Cardiorespiratory Stimulants, Arch. internat. de pharmacodyn. et de thérap. **42**: 200, 1932. (*g*) Behrens, B., and Reichelt, E.: Comparison of Cardiazol and Coramine in Animal Experiments, Klin. Wchnschr. **12**:1860, 1933. (*h*) Hicks, C. S.: Comparison of Action of Metrazol and Coramine on the Respiratory Center of Man, Australian J. Exper. Biol. & M. Sc. **13**:261, 1935. (*i*) Hofmann, H.: Effect of Cardiazol and Ephedrine on the Blood Pressure of Animals Depressed by Narcotics, Arch. f. exper. Path. u. Pharmakol. **183**:146, 1936. (*j*) Rice, J. C., and Isenberger, R. M.: Pharmacodynamic Reactions of Intracisternal Sodium Amytal, Coramine, Metrazol and Picrotoxin During Morphine-Sodium Amytal Anesthesia, J. Pharmacol. & Exper. Therap. **59**:43, 1937.

3. (*a*) Barker, M. H., and Levine, S. A.: Cardiazol: Some Experimental Effects of This Drug on the Cardiorespiratory Mechanism, Arch. Int. Med. **42**: 14 (July) 1928. (*b*) Camp, W. J. R.: Pharmacology of Cardiazol, J. Pharmacol. & Exper. Therap. **33**:81, 1928. (*c*) David, J. C., and Vareed, C.: Pharmacology of Metrazol, Indian J. M. Research **16**:920, 1929. (*d*) Watt, J. M.: Action of

(Footnotes continued on next page)

been advocated for the convulsive treatment of schizophrenia.[4] The drug has been shown to act on the spinal cord,[5] the medulla,[6] the central portions of the vegetative nervous system [7] and the somesthetic [8] and visual [3e] cortex. In contrast to strychnine, which acts on the sensory side of the reflex arc, metrazol affects the motor side of the synapse.[9] Buding,[10] on the basis of his studies on the central action of metrazol, classified this drug with the picrotoxin rather than with the camphor group of convulsants—a conclusion in accord with our findings that the effects of picrotoxin on the hypothalamus are similar in many respects to those produced by metrazol.[11]

SUMMARY

The effects of the intravenous or the intradiencephalic injection of a 10 per cent solution of metrazol on the spontaneous behavior and the hypothalamic reactions of 15 cats were studied in separate series of anesthetized and survival preparations. The results indicate:

1. The rapid intravenous injection of 0.6 cc. or more of a 10 per cent solution of metrazol in survival preparations causes tonic and clonic convulsions associated with apnea and evidences of widespread stimulation of the vegetative nervous system.

2. In animals anesthetized with ether, the blood pressure either falls or remains unchanged for ten or fifteen seconds after the intravenous

---

Metrazol on Cardiovascular System, Arch. internat. de pharmacodyn. et de thérap. **36**:225, 1929. (*e*) Fischer, M. H., and Lowenbach, H.: Stimulating Action of Metrazol in Animal Experiments, Klin. Wchnschr. **13**:1401, 1934; (*f*) Action Currents of Central Nervous System Under Influence of Convulsants: II. Cardiazol, Caffeine and Others, Arch. f. exper. Path. u. Pharmakol. **174**:502, 1934.

4. (*a*) von Meduna, L.: Experiments on the Biologic Modification of the Course of Schizophrenia: Camphor and Cardiazol Attacks, Ztschr. f. d. ges. Neurol. u. Psychiat. **152**:235, 1935; (*b*) Therapy of Dementia Praecox by Production of Epilepsy with Metrazol, Arch. gen. di neurol., psichiat. e psicoanal. **17**:289, 1936.

5. Maloney and Tatum.[2f] Camp.[3b] David and Vareed.[3c]

6. Eichler and Hildebrandt.[2a] Voss.[2b] Gremels.[2d] Goworow and Speranskaja-Stepanowa.[2e] Behrens and Reichelt.[2g] Hicks.[2h] Camp.[3b] David and Vareed.[3c]

7. Franken.[2c] Camp.[3b] David and Vareed.[3c]

8. Silver, S.: Hyperalgesia Caused by Hypnotics: Mechanism of Its Modification by Morphine, Arch. f. exper. Path. u. Pharmakol. **158**:219, 1930.

9. Koll, W.: Antagonistic Action of Narcotics and Analeptics on the Central Nervous System: Experiments with Metrazol and Strychnine on the Spinal Cord of the Cat, Arch. f. exper. Path. u. Pharmakol. **184**:365, 1937.

10. Buding, E. S.: Pharmacologic Classification of Metrazol on the Basis of Its Action on the Central Nervous System, Arch. f. exper. Path. u. Pharmakol. **157**:143, 1930.

11. Masserman, J. H., and Rodholm, A. K.: The Effects of Picrotoxin on the Hypothalamus of the Cat, to be published.

injection of metrazol, but vascular tension invariably mounts during the ensuing convulsion.

3. The intravenous administration of 1 cc. of a 10 per cent solution of metrazol does not affect the electrical reactions of the hypothalamus to a degree detectable by our methods.

4. The injection of from 0.05 to 0.1 cc. of the solution of metrazol into the hypothalamus of a recovery preparation induces loud vocalizations, manifestations of marked vegetative stimulation, great motor restlessness and vicious combative reactions to manipulation; however, convulsions of the skeletal musculature do not occur.

5. In animals anesthetized with ether, the intrahypothalamic injection of from 0.05 to 0.1 cc. of the solution of metrazol induces similar skeletal motor and vegetative discharges, definitely lightens the anesthesia and causes an increase in the intensity of the responses to both homolateral and contralateral faradic stimulation of the hypothalamus.

Metrazol therefore stimulates the vegetative and emotional mimetic functions of the hypothalamus when applied directly to this region of the diencephalon.

CARDIAC ACTIVITY DURING EPILEPTIC SEIZURES

THEODORE C. ERICKSON, M.D.
MONTREAL, CANADA

In spite of the considerable attention which has been devoted to the effect of epilepsy on the cerebral circulation, relatively little serious study with the methods of mechanical recording at present available has been made of the general circulation during an attack. It is particularly desirable to have concrete evidence as to the state of the peripheral circulation during a seizure so as to interpret the local vascular changes observed in the brain.

Gowers [1] in 1888 stated: "The pulse may be feeble at the onset but I have never noted an initial failing, although I have several times had my finger on the pulse when the fit came on." On the other hand, Russell [2] in 1906 from digital palpation reported cessation of the pulse during the onset of the epileptic fit.

Munson [3] in 1908 in 10 cases and Gibson, Good and Penny [4] in 1910 in 2 cases used mechanical recording from a sphygmomanometer cuff around the arm. The cuff was adjusted to a pressure just below the minimum blood pressure so that the pulse rate might be recorded. Munson concluded that cardiac arrest does not occur and stated that in his studies, except for a slight acceleration and in 1 case a slight slowing, the heart did not take part in the convulsion. Gibson, Good and Penny said that each of their patients was "in a fit" and was unconscious before any recognizable change was evident in the tracings of the pulse rate or in the blood pressure. None of their records in cases of idiopathic epilepsy show a lowering of general blood pressure sufficient to suggest that cerebral anemia from a general cause could have produced the convulsion, as it does, for instance, in the presence of the Stokes-Adams syndrome, in which the convulsions occur several seconds

---

From the Montreal Neurological Institute.

1. Gowers, W. R.: Diseases of the Nervous System, London, J. & A. Churchill, 1888, vol. 2, p. 686.

2. Russell, A. E.: Cessation of the Pulse During the Onset of Epileptic Fits, Lancet **2**:152-154, 1906.

3. Munson, J. F.: The Heart's Action Preceding an Epileptic Seizure, J. A. M. A. **50**:681-682 (Feb. 20) 1908.

4. Gibson, A. G.; Good, T. S., and Penny, R. G.: The Pulse Immediately Preceding the Epileptic Attack, Quart. J. Med. **4**:1-6, 1910.

after the pulse has stopped. They concluded that one must look for the mechanism of the fit in a local vasospasm of the brain rather than in a general cause, such as lowering of blood pressure from cardiac inhibition or splanchnic dilatation.

There have been few other clinical studies of changes in the circulatory system during or immediately preceding an attack, although there have been many studies of such changes in the interim between attacks (Felsen,[5] Hartenberg[6] and others). Lennox and Cobb[7] stated that during a seizure the blood pressure is greatly elevated and after a seizure it is lower than before. They have obtained electrocardiographic records of patients "during petit mal and myoclonic seizures." Neither the rhythm nor the amplitude of the waves was appreciably affected.

To be distinguished from the changes in the ordinary case of epilepsy are the changes in the general circulation in a case of autonomic epilepsy. In the case reported by Penfield[8] in 1929 the pulse was strong and rapid and the systolic blood pressure rose from 110 to 210. Observations such as those of Hirsch,[9] describing unilateral capillary dilatation in the nail beds on microscopic examination of the skin, are interesting as emphasizing the unilateral autonomic features in an occasional case but do not determine whether change in the general circulation has a causal relation to the attack.

The following observations are of interest. Winternitz[10] for several days after the occurrence of status epilepticus in 1 patient observed changes in the electrocardiogram, a long RT segment (0.42 seconds) and a total cycle of 0.68 second, indicative of closure of the coronary vessels. Gruber and Lanz[11] observed ischemic necrosis of the myocardium in an epileptic patient who died during an attack. Neubürger[12] reported 5 cases of genuine epilepsy in which the patients died in attacks

5. Felsen, J.: Laboratory Studies in Epilepsy, Arch. Int. Med. **46**:180-217 (Aug.) 1930.

6. Hartenberg, P.: La pression artérielle chez les épileptiques, Presse méd. **28**:748 (Oct.) 1920.

7. Lennox, W. G., and Cobb, S.: Epilepsy, Harvard Medicine Monographs, Baltimore, Williams & Wilkins Company, 1928.

8. Penfield, W.: Diencephalic Autonomic Epilepsy, Arch. Neurol. & Psychiat. **22**:358-374 (Aug.) 1929.

9. Hirsch, E.: Halbseitenerscheinung des Kapillarbildes bei einer Epilepsie, Med. Klin. **21**:48-50 (Jan. 11) 1925.

10. Winternitz, M.: Myokardnekrose nach Status epilepticus, Med. Klin. **29**: 1080-1081 (Aug. 4) 1933.

11. Gruber, G. B., and Lanz, H. F.: Ischämische Herzmuskelnekrose bei einem Epileptiker nach Tod im Anfall, Arch. f. Psychiat. **61**:98-102, 1919.

12. Neubürger, K.: Ueber Herzmuskelveränderungen bei Epileptikern, Verhandl. d. deutsch. path. Gesellsch. **23**:487-491, 1928; cited by Eufinger and Molz[14] and by Winternitz.[10]

and in which autopsy showed small or large myocardial scars but normal coronary vessels. These findings have been criticized by Winternitz and others on the basis of lack of normal controls.

Kisch [13] expressed the opinion that the myocardial damage often observed to follow status epilepticus is due to incomplete oxygenation. Eufinger and Molz,[14] in studying the electrocardiogram in the presence of pregnancy, obtained a tracing just after the patient had had an epileptic attack, while she was still unconscious. This tracing showed a Pardee Q complex, which signifies damage to the myocardium. One hour later the electrocardiogram showed normal conditions. Lewis [15] found that 30 per cent of a series of patients with epilepsy had hearts weighing less than the average, and Lennox and Cobb stated that patients with epilepsy do not have disease of the heart or arteries any more frequently than other ambulatory patients. In 423 autopsies at the Craig colony, hypertrophy of the heart was observed in 9 per cent.

Etienne [16] mentioned that in 1 epileptic seizure the heart sounds could be heard even though the pulse disappeared at the wrist. Orzechowski [17] in a discussion of the relation of the autonomic nervous system to the pathogenesis of epilepsy has reviewed some of the literature dealing with the vascular system in the epileptic patient. Padilla and Cossio [18] observed cessation of cardiac activity for six seconds at the onset of an epileptic seizure. Cases of the Stokes-Adams syndrome (in which loss of consciousness occurs eight or ten seconds and convulsions fifteen seconds after the onset of asystole) have been described in the literature as cases of genuine epilepsy. It is important to recall that convulsions may be associated with paroxysmal tachycardia (Barnes, 1926 [19]) and with the Stokes-Adams syndrome.

---

13. Kisch, F.: Das Elektrokardiogram Herzkranker beim inspiratorischen Atemanhalten, Klin. Wchnschr. **13**:686-689 (May 12) 1934.

14. Eufinger, H., and Molz, H.: Ueber das Auftreten eines Pardee-Q im epileptischen Anfall, Klin. Wchnschr. **13**:1177 (Aug. 18) 1934.

15. Lewis, N. D. C.: The Constitutional Factors in Dementia Praecox, with Particular Attention to the Circulatory System and to Some of the Endocrine Glands, Nervous and Mental Disease Monograph 35, Washington, D. C., Nervous and Mental Disease Publishing Company, 1923.

16. Etienne, G.: Le rôle des spasmes vasculaires, des troubles endocriniens et des troubles vago-sympathiques dans la pathogénie de l'épilepsie, Rev. neurol. **1**: 1317-1321 (June) 1932.

17. Orzechowski, K.: Relationship of the Autonomic Nervous System to the Pathogenesis of Epilepsy, Arch. Neurol. & Psychiat. **38**:16-26 (July) 1937.

18. Padilla, T., and Cossio, P., Jr.: Epilepsie, ausgelöst durch vollständiges Sistieren der Herztätigkeit, Zentralbl. f. d. ges. Neurol. u. Psychiat. **58**:693. 1930-1931.

19. Barnes, A. R.: Cerebral Manifestations of Paroxysmal Tachycardia, Am. J. M. Sc. **171**:489-495 (April) 1926.

Since Penfield [20] observed and reported cessation of cerebral pulsation during convulsions occurring when the brain was exposed by craniotomy, it was considered of prime importance to obtain more concrete evidence as to the state of the general circulation before and during a convulsion.

MATERIAL AND METHOD

The present report concerns mainly the electrocardiographic picture in the presence of spontaneous attacks of idiopathic epilepsy and other forms of epilepsy and in the presence of attacks induced during cortical stimulation at operation on epileptic subjects for the removal of a tumor or a cerebral cicatrix. In most cases only one lead was taken, and this had to be chosen so that the electrodes would not pick up too many electrical effects from the muscles during the convulsion. A direct chest lead was used, one electrode being placed over the manubrium sterni just below the sternal notch and the other just below the point at which the apex beat of the heart was palpated. The electrodes were connected to the input of a two stage amplifier designed and built by B. H. C. Matthews.[21] Photographic records were taken from a Shire oscillograph.

RESULTS

Satisfactory electrocardiographic tracings were obtained during 54 epileptic seizures of various types in 17 different patients. In many cases the recording began with the aura, several seconds before onset of the attack proper. In other cases recording began one or two seconds after the first objective symptoms of the attack had appeared. Of the 54 attacks, 23 were entirely spontaneous, 11 occurred while the patient was being treated with a hydration regimen, 18 were induced by stimulation of the cerebral cortex during craniotomy and 2 were induced by hyperpnea. Electrocardiograms of many other epileptic patients were taken, but there was no success in obtaining records during a convulsion. Four of the attacks during which satisfactory tracings were obtained were severe generalized convulsions of the typical grand mal type, 8 were typical petit mal seizures and 1 was a psychomotor attack. The remainder were attacks of jacksonian epilepsy with various degrees of spread. It is to be emphasized that no case of autonomic epilepsy is included in this study.

The cardiac rate as judged from these records most frequently showed acceleration. In fact, acceleration was observed in all the patients studied in 1 or more attacks, although not in all attacks. In some attacks there was no change of rate, in others the acceleration was about 10 per cent, and in 1 patient the rate rose from 92 before the attack to 180 during the attack. The mild attacks generally caused

20. Penfield, W.: The Evidence for a Cerebral Vascular Mechanism in Epilepsy, Ann. Int. Med. **7**:303-310 (Sept.) 1933.

21. Matthews, B. H. C.: A Special Purpose Amplifier, J. Physiol. **81**:28P-29P (May 21) 1934.

only slight change in cardiac rate (acceleration of 10 per cent more or less), while the severe attacks showed marked acceleration (from 38 to 100 per cent). In 2 attacks slowing of the rate was observed during the attack, and not infrequently there was also a relative slowing after it.

In none of the 54 attacks observed was there any dropping out of the QRS interval of the electrocardiogram. In all except 4 patients the T wave was unchanged during the attack. It is generally recognized that the early part of the QRS deflection is due to impulse conduction, but it has been shown by Bartos and Burstein [22] that the QT interval can be used as a rough index of ventricular systole. In 4 cases the T wave became biphasic or flattened at the end of the attacks, apparently owing to deficient oxygenation of the myocardium following a period of apnea and cyanosis. It has been suggested by Dr. R. G. Brow that administration of pure oxygen during the attack might eliminate this change and thus prove its causation. No opportunity has yet been found to carry this out. Dr. Brow suggested also that such changes might occur in a patient who has had some slight coincidental myocardial damage. The reports of myocardial damage which have been made from both autopsic and electrocardiographic evidence are not important when one is considering the pathogenesis of the epileptic seizure. They are probably secondary to the onslaught of the attack (perhaps the result of deficient oxygenation), for the changes which my associates and I have observed in the T waves occurred only late in the attack, after a period of apnea.

Tracings of the pulse rate obtained by means of a finger plethysmograph connected to a tambour were obtained by Dr. Exum Walker in 12 attacks, and in none was there a cessation of pulse. The heart was auscultated during 21 attacks. In 19 there was slight acceleration, and in 2 the beat could not be heard because of extraneous noises.

Reliable observations of the blood pressure were obtained during 8 convulsions in 3 different patients. Of these 8 seizures, 4 (relatively small attacks) caused no change in blood pressure. Two attacks during which the blood pressure rose were very severe, as were 2 which showed a fall of blood pressure. This is in accord with the findings for convulsions experimentally produced in animals (Coombs and Pike [23]). It may represent the same mechanism as was observed in Valsalva's and Müller's experiments and may be accounted for by asphyxia in variable degree, or it may represent variable autonomic involvement.

---

22. Bartos, E., and Burstein, J.: Can Variations in Ventricular Systole Be Determined from Electrocardiogram Deflections? J. Lab. & Clin. Med. **9**:217-228 (Jan.) 1924.

23. Coombs, H. C., and Pike, F. H.: Respiratory and Cardiovascular Changes in the Cat During Convulsions of Experimental Origin, Am. J. Physiol. **97**:92-106 (Jan.) 1931.

The pulse at the wrist was reported to be absent or fading in 24 attacks observed by me when simultaneous electrocardiographic tracings or tracings of the pulse rate showed no changes. In 3 patients the pulse could not be palpated on the side on which a unilateral convulsion occurred but on the uninvolved side the radial pulse was easily palpated throughout the attack. The only conclusion to be drawn is that muscular contraction and movement locally under the palpating finger or higher by occlusion of the subclavian artery make it impossible at times for even a trained observer to palpate the pulse at the wrist.

The electrocardiogram was unchanged during 7 attacks in which the patient was on the operating table and in which there was disappearance of cerebral pulsation. Satisfactory electrocardiograms were obtained throughout 18 convulsions induced by cortical stimulation. In 7 of

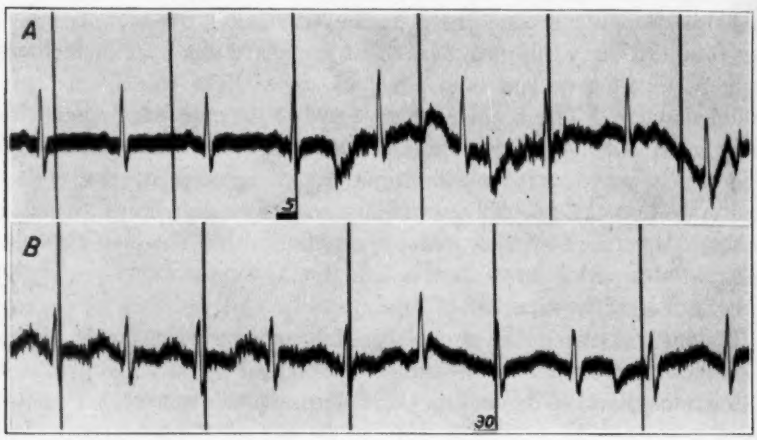


Fig. 1.—Samples from a continuous electrocardiographic tracing beginning before and continuing throughout a convulsive seizure produced by stimulation of the cortex during a craniotomy (patient C. M., aged 22; diagnosis, jacksonian epilepsy). Strip *A* shows the period of onset, the marker indicating a point of time five seconds after the first evidence of the attack and disappearance of cerebral pulsation. Strip *B* covers the end of the attack. Cerebral pulsation returned at the signal (thirty seconds).

these attacks Dr. Penfield and his assistants observed definite cessation of cerebral pulsation, while the electrocardiogram in no case showed asystole.

REPORT OF CASES

The case of patient C. M., a woman aged 22, is illustrative. A parieto-occipital craniotomy on the right was performed, with the aid of local anesthesia, on May 11, 1937, by Dr. W. Penfield. The electrocardiographic record (fig. 1) began five seconds before the vocalization and startled expression which marked the onset of the attack. This was followed by turning of the head and eyes to the left and

by clonic movements in the left upper extremity. The attack lasted thirty-five seconds, and pulsation returned in the brain and the wrist at about the same time, having been absent from the onset. It is to be noted that in spite of the cessation of cerebral pulsation no asystole was recorded in the electrocardiogram. The only changes observed were the extraneous muscle potentials.

Another illustrative case is that of F. H., a man aged 25, on whom an osteoplastic craniotomy on the right and removal of a meningocerebral cicatrix were done, with the region under local anesthesia, on Sept. 25, 1937, by Dr. Penfield. By stimulation with the thyratron stimulator a focus for the attacks was demonstrated just above the cicatrix and just below the hand area. Electrocardiograms were obtained during 3 attacks, and 1 of these is presented (fig. 2). Dr. Penfield's notes at the time of operation were: "The attack took place on restimulation of not more than fifteen seconds' duration. The pulse in the arteries of the brain disappeared for eleven seconds and that in the wrist for ten seconds. This was only in the left wrist on the side on which the attack occurred. Dr. Erickson

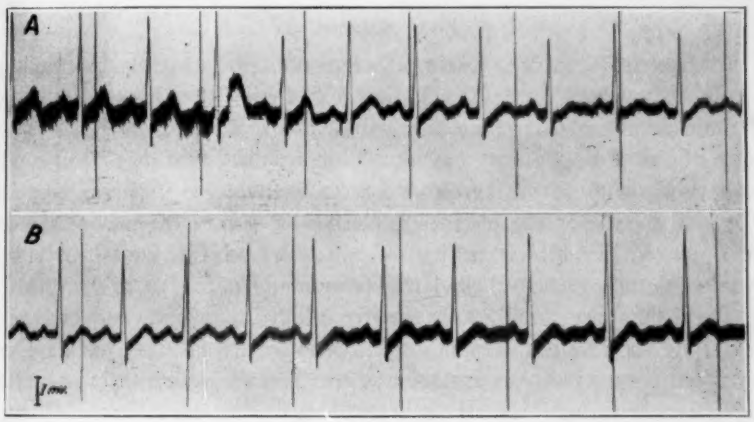


Fig. 2.—Samples from an electrocardiographic record beginning before and continuing throughout an epileptic seizure induced by cortical stimulation with a thyratron stimulator. The patient (F. H.) was a man aged 25 with a meningocerebral cicatrix. Strip *A* was selected from the record taken during cortical stimulation and the onset of the seizure. The period of the cortical stimulation is indicated by the increase of basal vibration produced by the 60 cycle thyratron stimulator. Strip *B* immediately follows *A* and shows the end of the very short (ten seconds) but very severe attack described in the text.

was able to palpate the pulse in the right wrist throughout. There was shaking of the left arm. During the attack the head was turned to the left and backward. The left eye was turned to the left (the right eye was covered). The patient reported the 'same kind of attack.'" The increase of basal vibration at the beginning (fig. 2) was the result of the cortical stimulation by the 60 cycle thyratron and acted as a marker. Changes in the T wave were evident, but there was no asystole even though cortical pulsation was absent and the radial pulse impalpable on the convulsed side during the period shown on the record.

It can be stated with certainty that the cessation of cerebral pulsation during a convulsive seizure is not the result of cardiac asystole. It

may be due to changes in the general circulation, e. g., a low pulse pressure with an unchanged systolic pressure, but it seems more probable that it is due to local changes in the cerebral circulation. No direct measure of pulsation or pressure of the internal carotid artery during seizures is as yet available. The results of the present electrocardiographic studies of the heart during epileptic seizures, while they yield essentially negative results from a pathogenic standpoint, do help to clarify a rather confused situation. Disappearance of the radial pulse, so often reported by good observers, undoubtedly occurs, as we ourselves have sometimes seen, but simultaneous electrocardiographic tracings show that this is not due to cardiac asystole. It is due rather to movement or increase of tension of the muscles or tendons underlying the palpating finger or to occlusion of the subclavian artery by muscular contraction.

SUMMARY

Electrocardiographic tracings were obtained during 54 epileptic seizures of various types (excluding autonomic diencephalic epilepsy). In none of these was there any evidence of asystole, even though in many of the attacks there was simultaneous disappearance of the pulse at the wrist and in the cerebral cortex during operation. Disappearance of the pulse at the wrist is explained by increased muscular movement or tension interfering with palpation of the radial artery or actually occluding the subclavian artery in the neck.

The heart rate during an epileptic seizure may show no change or may show acceleration, depending on the severity of the attack. Occasional temporary changes are seen in the T wave, apparently secondary to deficient oxygenation of the myocardium during the seizure. Changes in the blood pressure during convulsions are variable and perhaps are produced by various mechanisms. Disappearance of cerebral pulsation during convulsions cannot be due to cardiac asystole or changes in the general blood pressure; hence it must be due to other general or to local factors.

ELECTROENCEPHALOGRAPHY IN CLINICAL NEUROLOGY

ITS VALUE IN ROUTINE DIAGNOSIS

DENIS WILLIAMS, M.D., M.R.C.P.
LONDON, ENGLAND
AND
FREDERIC A. GIBBS, M.D.
BOSTON

In 1931 Berger [1] showed that impairment of cortical function resulting from high intracranial pressure in man is associated with the appearance of abnormally slow electrical potentials of about 3 a second. These potentials were recorded through the intact skull by placing electrodes on the forehead and occiput. The method he used was similar to that with which he originally demonstrated the normal 10 a second rhythm. Two years later,[2] he found similar slow waves confined to the affected hemisphere in 2 cases of cerebral tumor. He was unable to obtain the abnormally slow waves when the tumor was situated midway between his electrodes, but they appeared when one of the electrodes was in proximity to it. In 1935, Kornmüller [3] and Foerster and Altenburger [4] showed that the slow alternating potentials do not originate in cerebral tumors themselves. It appeared, therefore, that the disturbances were arising in the surrounding cerebral tissue, the activity of which was being modified by the mechanical or metabolic disturbance of the neoplasm. This was borne out by Dusser de Barenne and McCulloch,[5]

Aid for this study was received from the Rockefeller Foundation.

A preliminary report on this investigation was presented at a meeting of the Boston Society for Psychiatry and Neurology, March 17, 1938.

Work undertaken in the Department of Neurology of Harvard University, and in the Neurological Unit of the Boston City Hospital during tenure of a Rockefeller Traveling Fellowship in Neurology.

1. Berger, H.: Ueber das Elektrenkephalogramm des Menschen, Arch. f. Psychiat. **94**:16, 1931.

2. Berger, H.: Ueber das Elektrenkephalogramm des Menschen, Arch. f. Psychiat. **100**:301, 1933.

3. Kornmüller, A. E.: Die bioelektrischen Erscheinungen architektonischer Felder der Grosshirnrinde, Biol. Rev. Cambridge Philos. Soc. **10**:383, 1935.

4. Foerster, O., and Altenburger, H.: Elektrobiologische Vorgänge an der menschlichen Hirnrinde, Deutsche Ztschr. f. Nervenh. **135**:277, 1935.

5. Dusser de Barenne, J. G., and McCulloch, W. S.: Some Effects of Laminar Coagulation upon the Local Action Potentials of the Cerebral Cortex of the Monkey, Am. J. Physiol. **114**:692, 1936.

who produced slow waves by coagulating the cortex, and by Bishop,[6] who found similar potential changes when he recorded from the cortex after he had made a subcortical section.

Walter [7] modified a technic which had been evolved by Adrian and Matthews [8] and used by Adrian and Yamagiwa [9] to localize the site of origin of the 10 a second rhythm. With it he recorded the differences in potential between areas of cortex a few centimeters apart and localized a focus of origin of slow waves at a point on the skull under which a cerebral tumor was subsequently observed to have invaded cortex. He therefore applied the technic to a group of cases in which a cerebral tumor was suspected and predicted the correct position of the tumor in 3 instances. He extended his investigations and later [10] successfully localized the site of a tumor in 12 cases. In 26 cases in which cerebral tumor was suspected on clinical grounds and in which he was unable to demonstrate a focus of slow activity, the subsequent investigation and course of the disease did not substantiate the original clinical diagnosis.

Thus, apart from the physiologic significance of these slow waves, it appeared that a highly accurate diagnostic method was available to the clinician in a field which was notorious for its pitfalls. No apology is necessary for such a method, for clinical localizing signs may be so indefinite that it is impossible to determine without ancillary methods whether papilledema has been caused by high intracranial pressure resulting from internal hydrocephalus or from a neoplasm in the frontal region. The anxiety that the neurosurgeon feels is reflected in the widespread use of such radical diagnostic methods as ventriculographic, encephalographic and arteriographic examination. If a new method would enable him to plan his operation with greater certainty and would be without danger or discomfort to the patient, it would soon have an established place in clinical investigation.

Although the electroencephalogram was being widely used to investigate the normal and pathologic physiology of cerebral activity, it appeared that its importance to clinical neurology had not been fully appreciated.

---

6. Bishop, G. H.: Interpretation of Cortical Potentials, in Cold Spring Harbor Symposia on Quantitative Biology, Cold Spring Harbor, L. I., New York, The Biological Laboratory, 1936, vol. 4, p. 305.

7. Walter, W. G.: The Location of Cerebral Tumours by Electro-Encephalography, Lancet **2**:305, 1936.

8. Adrian, E. D., and Matthews, B. H. C.: The Berger Rhythm: Potential Changes from the Occipital Lobes of Man, Brain **57**:355, 1934.

9. Adrian, E. D., and Yamagiwa, D.: The Origin of the Berger Rhythm, Brain **58**:323, 1935.

10. Walter, W. G.: The Electro-Encephalogram in Cases of Cerebral Tumor, Proc. Roy. Soc. Med. **30**:33, 1937.

It was therefore decided to use the method as a diagnostic procedure in a large neurologic clinic in order to assess its value under standard field conditions.

It is the purpose of this paper to describe the methods used and the results obtained in this investigation. Dr. W. G. Lennox gave help and advice during the investigation.

METHOD

Prawdicz-Neminski,[11] in 1913, recorded alternating potentials from the exposed cortex of the dog. Little interest was taken, however, until Berger[12] demonstrated similar potentials through the intact skull in man in 1929. Interest steadily grew, until today, less than ten years later, the amplifying and recording systems used are so well known that detailed technical description is unnecessary.

Briefly, the method involves the use of electrodes placed on the scalp, connected to a series of independent condenser-coupled amplifying systems. These activate separate cathode ray or ink-writing oscillographs, which record on moving paper. The device should be capable of undistorted recording of alternating potentials of about 2 to 3 microvolts, with frequencies ranging from 1 to 60 a second. Practical points will be discussed later.

Electrodes.—Many models of electrodes have been devised. They are of two main types, metal electrodes fixed to the scalp and readily movable pad electrodes moistened with a solution of sodium chloride. The former are of value when continuous records are required which must be compared over long periods or when the patient is uncooperative. A flat plaque of solder, about 5 to 10 mm. in diameter, forming a contact with the scalp through a little electrocardiographic electrode paste and fixed to the scalp with collodion or any other adhesive, is quite as serviceable as the more elaborate types. The small amount of polarization resulting from the minute current flowing does not appreciably modify the alternating potentials recorded. Although it is admirable for continuous and exact recording of brain potentials, this electrode system is tedious when used for exploring the scalp carefully, as placing and removing the electrodes is time consuming.

The great advantage of saline pad electrodes in the localization of lesions by the electroencephalographic method is that the position of such electrodes can be rapidly changed. Here again, the more elaborate types have no practical advantage over the simpler ones. A serviceable electrode and the means of holding it on to the scalp have been described by Walter.[10] The electrode is placed on the scalp, care being taken to separate the hair so that a good contact is made. It may be necessary to clean the scalp in contact with the electrode with alcohol or ether if it is greasy, or with solution of sodium chloride if the hair is dry and crisp. In most cases, however, a direct current resistance of 15,000 ohms or less can be obtained without this precaution. This gives satisfactory recording.

---

11. Prawdicz-Neminski, W. W.: Ein Versuch der Registrierung der elektrischen Gehirnerscheinungen, Zentralbl. f. Physiol. **27**:951, 1913.

12. Berger, H.: Ueber das Elektrenkephalogramm des Menschen, Arch. f. Psychiat. **87**:527, 1929.

The greatest disadvantage of this type of electrode is that artefacts are likely to arise as the result of slight movement of the contact surface on the scalp or by drying of the saline pad. Drying causes slow sways in the recording base line, and the static changes in dry hair produce sharp monophasic spikes resembling condenser discharges. Occasionally, electrodes placed in the occipital and temporal regions will be so displaced by a superficial artery that the pulsations may simulate slow cortical potentials. This may occur if the pad or the foot is near the artery. Slight adjustment of the electrode will disclose the true cause of the rhythmic changes in potential.

Electrode Placement.—Two electrode systems are available for use. They give fundamentally different records and serve different purposes. One, described by Tönnies,[13] employs a single electrode placed on the scalp and an "indifferent" electrode placed on a relatively inactive area, such as the ear. This indifferent electrode is grounded. This system reflects the potential changes of the area under the scalp electrode with reference to ground. It is a fairly good indication of the true potential changes of that one small cortical area. This will be referred to as the "single scalp electrode" system (fig. 1).

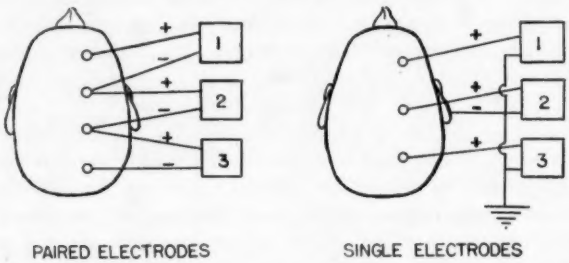


Fig. 1.—Diagram of the two recording systems described in the text. On the left, four electrodes placed in line on the right side of the head are connected in pairs to three amplifying systems, numbered *1, 2* and *3*. These systems are quite independent. It will be seen that the middle electrodes are each connected to two amplifiers, supplying the negative lead of one and the positive lead of the next. On the right, three electrodes over the same area of the head are connected to three similar amplifying systems, which are connected through a common grounded lead in contact with an indifferent point, the ear.

The other system, used by Adrian and Walters, employs a pair of electrodes on the scalp which are both connected to the input of an ungrounded amplifier. The input of the amplifier is balanced so that the record obtained is the result of the difference in potential between the two areas of cortex. Thus, if the potential at the two points changes by the same amount the change is canceled out and causes no deflection of the recorder. If, however, the potential under one electrode alone changes the potential difference so produced is reflected in the record. This system will be referred to as that of "paired electrodes" (fig. 1).

If a potential gradient from a point is visualized as a hill, the single scalp electrode records the height of the hill above the flat ground level, while the

13. Tönnies, J. F.: Die unipolare Ableitung elektrischer Spannung vom menschlichen Gehirn, Naturwissenschaften **221**:411, 1934.

paired electrodes measure the difference between two points on the hill without any reference to the absolute height of either of the points.

In the present investigation both single and double electrodes were used simultaneously in many cases, recording absolute changes in potential and also differences in potential between points on the cortex. It was seen that a much truer reproduction of a pure wave form was obtained with single than with paired electrodes. This was clearly demonstrated in a petit mal seizure, when the pure spike and wave formation which was apparent in the single scalp electrode system rapidly became distorted in the paired electrode system. On the other hand, with paired electrodes on the scalp changes in potential under one electrode were much more apparent than when two scalp electrodes were feeding into two independent grounded amplifiers. The reason for this is that with paired electrodes all the changes in potential common to both were canceled out, so that the local discharges stood out in isolation. For this reason, this method is of great value in the localization of foci. If a series of such paired electrodes is placed across the scalp in a straight line, as described by Adrian and Yamagiwa,[9] the origin of a focus of discharge is at once more evident. Pursuing the analogy of the hill, if the hilltop is under any one electrode the potential gradient will fall off in all directions from that electrode. If it is at the end of the row of electrodes all the other electrodes will be on the same side of the hill, so that the potential will fall in the same direction in each pair and so cause a deflection of each of the recorders in the same direction. If the hill is at one of the middle electrodes the fall will be away from the electrode in both directions and so will pass through the circuits on each side in opposite directions, making an upward signal on one recorder and a downward signal on the other. Therefore, if in such a system a difference in phase is found in two records it is apparent that the discharge must have originated between the pairs of electrodes supplying the systems. When ungrounded balanced input circuits are used a series of amplifying systems can record independently at the same time. It is therefore possible in using a row of electrodes such as has been described to replace two adjacent electrodes by one which is common to two neighboring amplifiers. Thus, the number of electrodes is reduced and the method simplified. These principles, which are fundamental to the method of localization used in this work, have been fully demonstrated by Walter.[10] They are diagrammatically represented in figure 2.

Amplifiers.—At least three independent condenser-coupled amplifying units incorporating a balanced input circuit in the preamplifier stage are necessary. Types of circuit in use have been described by Adrian and Matthews [8] and by Jasper and Andrews.[14] Well grounded and insulated shielding of the apparatus and also of the patient will probably be necessary in spite of the "push-pull" circuit used, as alternating current, roentgen rays and diathermy are usually in close proximity to any electroencephalograph in clinical use. With this precaution, if one has good amplifiers, the noise level can be kept below 2 to 3 microvolts.

For clinical use it is probable that recording with an ink-writing oscillograph is more serviceable than with a cathode ray tube, as continuous records may be kept at negligible cost and no frequencies of value in the investigation of abnormal cerebral states have yet been demonstrated which cannot be handled efficiently by a good ink-writing oscillograph. If there is doubt as to the true wave form, a cathode ray tube can readily be substituted.

---

14. Jasper, H. H., and Andrews, H. L.: Human Brain Rhythms: I. Recording Techniques and Preliminary Results, J. Gen. Psychol. **14**:98, 1936.

The amplifiers and ink-writing oscillographs used in this investigation were designed and built by A. M. Grass.

Procedure.—It is most convenient to have the subject seated, but records can be obtained from bedridden and comatose patients. Four pad electrodes moistened with a solution of sodium chloride leading to three amplifiers (fig. 1) are placed on the scalp in predetermined positions. In exploring the head it is well to adopt a standard set of electrode placements to include records from all over the scalp in as few moves as possible. Right and left frontal, parietal and occipital areas may be compared in turn with the electrodes placed coronally, or each hemisphere may be explored independently with two rows of electrodes running sagittally.[10] The method is illustrated in figure 3, *A* to *E*, inclusive.

If the amplifying systems are calibrated against a known signal and the resistance of each pair found to be of the same order, the size as well as the frequency and phase relationships of the three simultaneous records can be compared.

These precautions having been taken, an abnormality may be observed in one of the records. When the position of the abnormality has been roughly localized,

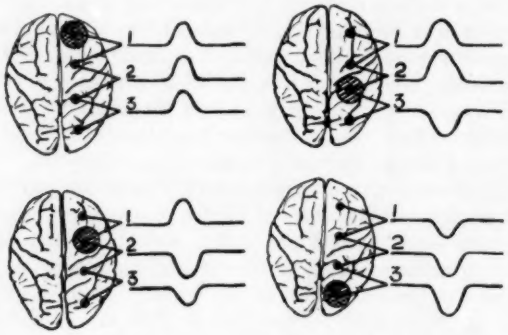


Fig. 2.—Four electrodes are connected to three amplifying and recording systems in the same manner in each case. An electrical discharge of constant sign under each electrode causes a deflection of the recording pen in the direction shown. It is therefore possible, by studying the phase relationships of the waves recorded, to determine under which electrode the disturbance has occurred.

the electrodes can be approximated until a more accurate localization of the discharge can be made. Differences in phase of abnormal waves have been observed with the electrodes placed less than 2 cm. apart (fig. 4).

MATERIAL

All the patients used in this investigation had symptoms or signs referable to the central nervous system. Except as stress was laid on the desirability of investigating patients who might have cerebral lesions or who suffered from some form of epilepsy or allied changes in behavior, selections were made at random from the patients admitted to the hospital.

The majority were referred from the neurologic and neurosurgical services of the Boston City Hospital by Dr. Tracy Putnam, Dr. Donald Munro and their

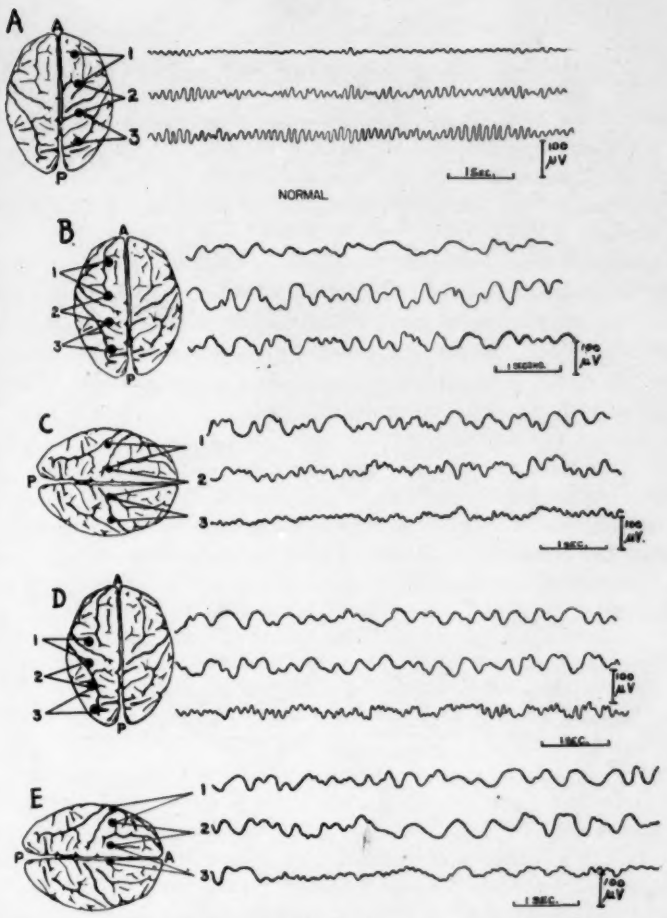


Fig. 3.—A series of samples of records taken from a subject with a left parieto-occipital focus of slow waves, to illustrate the method used in localizing the focus.

In all the figures, the horizontal line represents one second, and the vertical line, 100 microvolts. *A* represents the anterior part of the brain, and *P*, the posterior.

In *A*, four paired electrodes are shown in line from before backward on the right side. A normal 10 per second frequency, which is maximal in the occipital region, is seen. In *B*, four similar electrodes are shown on the left side. High voltage waves of 2 to 4 per second are present. They are most evident and are out of phase in the lower two records. This indicates that their origin is near the third electrode. In *C*, similar electrodes are placed from left to right. The slow waves are most evident in record *1*, and a few waves are seen to be out of phase in records *1* and *2*. This confirms the opinion that the lesion is on the left side. In *D*, the electrodes are moved closer together over the site of origin of the abnormal waves. They are now seen to be of high voltage and out of phase in records *1* and *2*. The focus is therefore under the second electrode. Ten per second waves, as well as low voltage 2 to 3 per second frequencies, are present in the third record. In *E*, the anteroposterior position of the lesion having been established, the electrodes are now moved at right angles. Two per second waves are out of phase in records *1* and *2* and are in phase in *2* and *3*. The lesion is therefore localized laterally and is a left parieto-occipital focus about midway between the vertex and the ear.

assistants. Some came from neurologists and neurosurgeons in other centers, and a few were from the medical wards of the hospital. Many of the patients were referred because the diagnosis was uncertain or the localization of a lesion indefinite or unknown. The patients from the outside clinics were highly selected in this respect.

The clinical diagnosis was unknown to the investigators, and as far as possible, the study was made in ignorance of the clinical findings. After a report had been made on the electroencephalographic findings, these were correlated with the clinical data. When advisable the patients were then reexamined in an attempt to extend the results or to explain discrepancies. In some cases the clinical course was checked with repeated electroencephalograms.

One hundred and five patients were investigated for evidences of local cortical damage. They were included in a consecutive series of 660 subjects investigated by electroencephalographic methods in ten months. This large group included normal subjects drawn from the hospital staff and elsewhere, patients with organic diseases of the central nervous system, epileptic patients of all types, psychotic patients and children showing aberrations of behavior. The present investigation is concerned directly with the first group of 105 patients.

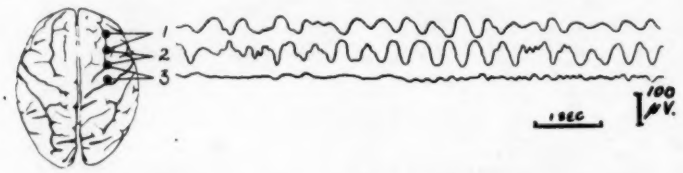


Fig. 4.—High voltage 3 per second "subclinical" seizure waves with a focus near the second electrode. They do not affect the third record, which shows a 10 per second frequency. The electrodes are less than 2 cm. apart over an area of cortical damage (see text).

RESULTS

Evidence of focal cerebral dysfunction was found in 64 of the 105 cases. The only absolute criterion of the accuracy of electroencephalographic diagnosis in these 64 cases would be the demonstration of the lesion at operation or autopsy. This was possible in 35 cases. In another group of 15 cases clinical evidence of localization was strong or was supported by the results of previous exploration, by roentgenographic evidence or by other signs of the lesion, such as a visible mass, skull defect or scalp wound, so that the diagnosis could be made with accuracy. It was therefore possible to establish the accuracy of this method of diagnosis in 50 cases. There were thus 14 cases in which, through lack of clinical and pathologic data, such evaluation was impossible. These were excluded from the series.

In the remaining 41 patients no evidence of a local organic focus was obtained. Six of these showed normal records, and the rest had cortical potentials which have been associated with the various types of epilepsy

(Gibbs, Davis and Lennox [15] and Gibbs, Lennox and Gibbs [16]). Some showed generalized abnormality and in others a focus of discharge was found similar to those described by Walter [17] and Gibbs [16] and their colleagues. The types of cortical potential seen in epilepsy have already been described in detail,[18] so that the main interest in this group of cases is that no focus of abnormal activity was found which could be dissociated from the epileptic discharge.

It is difficult to express the accuracy and scope of any clinical method in absolute terms. For practical purposes, the localization of a cerebral lesion to the central part of a cranial osteoplastic flap would be desirable. This arbitrary criterion will be used in assessing the accuracy of the method.

In 36 of the 50 verified cases a single focus of abnormality was presented; in 7 there were two foci, and in 7, generalized abnormal waves. All the single foci were correctly localized. The position of two electrical foci corresponding to two pathologic cortical areas was confirmed in 4 of 7 cases. In 2 other instances the major focus was found to be associated with a demonstrable lesion, and the possibility of another focus in the position indicated by the electroencephalogram was great, although it had not been localized by other methods. One of these patients had metastatic cerebral abscesses, and the other had two injuries to the head resulting in a hematoma, which was later removed. In the remaining patient there were generalized high voltage slow waves, as well as two foci of similar abnormal waves. The position of the major disturbance was correctly predicted, but the subsidiary focus was not observed until the record was reexamined after a second smaller lesion had been demonstrated at autopsy.

In 7 cases with generalized 3 a second waves in which no focus could be found, high intracranial pressure was present. Intravenous injection of a hypertonic solution of dextrose and sodium chloride reduced the amount of abnormal activity; as a focus was still not apparent, a diagnosis of high intracranial pressure without a localized supratentorial lesion was made. This was upheld in each of the cases by the demonstration of lesions in the posterior fossa (fig. 5).

Some of the 14 cases in which the pathologic process was not determined with certainty but in which abnormal slow waves were found are of interest, as they included 2 cases in which there were well marked foci diagnosed as acute encephalitis and 1 case of encephalitis periaxialis diffusa in which there was generalized abnormal activity, most marked in the occiput. In 5 of the cases cerebral tumor

15. Gibbs, F. A.; Davis, H., and Lennox, W. G.: The Electroencephalogram in Epilepsy and in Conditions of Impaired Consciousness, Arch. Neurol. & Psychiat. **34**:1133 (Dec.) 1935.

16. Gibbs, F. A.; Lennox, W. G., and Gibbs, E. L.: The Electroencephalogram in Diagnosis and in Localization of Epileptic Seizures, Arch. Neurol. & Psychiat. **36**:1225 (Dec.) 1936.

17. Golla, F.; Graham, S., and Walter, W. G.: The Electroencephalogram in Epilepsy, J. Ment. Sc. **83**:137, 1937.

18. Gibbs, Davis and Lennox.[15] Gibbs, Lennox and Gibbs.[16]

was suspected, and well defined foci of abnormal potentials were present. The rest were cases of injuries to the head.

The results obtained in the verified cases are listed in tables 1 and 2.

The tabulated results show a high degree of correlation between the predicted and the established position of the lesions. They do not, however, reflect the clinical aspects of the problems encountered. As records illustrating the clinical significance of the results have been published elsewhere (Williams and Gibbs [19]), individual cases will be referred to merely to illustrate points arising in the text.

Differential Interpretation of the Record.—(*a*) Extent of the Lesions: As the electrodes are placed on the intact skull there is diffusion of the cortical potentials through the meninges, calvarium and scalp, with resulting loss of fine details of localization of cortical frequencies. The wave form is identical with that obtained from direct cortical leads, but the voltage is lower (Tönnies [20]). A patient in

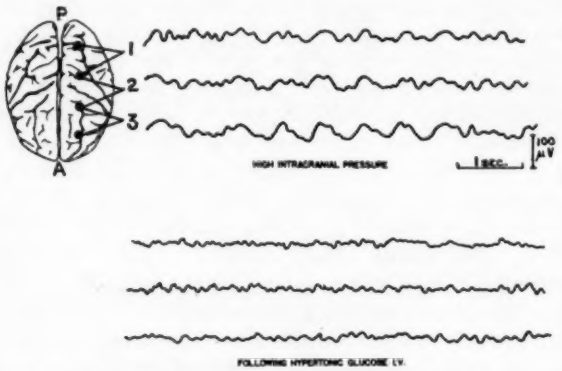


Fig. 5.—The electroencephalogram from a patient with a high intracranial pressure and a tumor of the posterior fossa. Two per second waves are present in all leads in the upper record. In the lower, taken twenty minutes after 50 cc. of a 50 per cent solution of dextrose and sodium chloride was injected intravenously, the slow waves have disappeared, and a 10 per second frequency is present.

this series with an injury to the head showed a localized abnormality which was observed at operation to be a small cortical cicatrix, which was excised. A high voltage wave with a frequency of about 3 a second was present in opposite phase in two adjacent pairs of electrodes, but no slow frequencies were present in the third pair. The electrodes were placed in line, 2 cm. apart. Localization can therefore be extremely accurate and the extent of a lesion thus delimited. It is usual to have a greater diffusion of high voltage slow activity than was present

19. Williams, D. J., and Gibbs, F. A.: The Localization of Intracranial Lesions by Electroencephalography, New England J. Med. **218**:998, 1938.

20. Tönnies, J. F.: Die Ableitung bioelektrischer Effekte vom uneröffneten Schadel: Physikalische Behandlung des Problems, J. f. Psychol. u. Neurol. **45**: 154, 1933.

in this case, but it should be possible in most cases to assess the extent of cortex producing abnormal frequencies to within 3 or 4 cm. In 1 case there was a large exostosis of the left parietal bone. With electrodes 2 cm. apart, a few low voltage slow waves were found in the middle of the exostosis. These waves were of lower voltage than the normal 10 a second rhythm and with the amplification generally used would probably have been unrecognized. At operation a meningioma was seen which was almost entirely limited to bone. It presented a smooth flat surface to the cortex, which appeared normal except for a small area, less than 1 cm. in diameter, which was adherent to an isolated nodule of tumor. Minute lesions can therefore be accurately localized.

Another subject was found to have high voltage slow waves of 2 or 3 per second all over the right frontal, parietal and temporal regions. These were found to be maximal in the frontal lobe and over an area roughly bounded by the rolandic and sylvian fissures. They were sharply limited by the sagittal sinus. A diagnosis of a uniform cortical disturbance with the limits described was made, and at opera-

TABLE 1.—*Accuracy of Electroencephalographic Diagnosis in 105 Cases*

Number of Cases	Cases in Which There Were Pathologic Foci, Excluding Those of Epilepsy	Cases in Which Pathologic Tissue Was Demonstrated
105	64	50

TABLE 2.—*Cases in Which Abnormal Foci and Lesions Were Demonstrated*

Type of Abnormality	Number of Cases	Number of Lesions or Foci Accurately Verified
Single focus	36	36 lesions
Two foci	7	13 foci
Generalized abnormality	7	7 lesions

tion an oval *meningioma en plaque,* the length of which was 10 cm. and the breadth 7 cm., was removed. The edges of the tumor corresponded closely with the estimated size of the lesion. It is thus apparent that any superficial lesion, if it is sufficiently discrete, can be outlined with some degree of accuracy through the intact skull.

(*b*) Depth of the Lesions: It has been shown that the alternating potentials normally recorded are cortical in origin and that damage to the cortex causes slower frequencies to appear (Dusser de Barenne and McCulloch [5]). It would be expected, therefore, that cortical damage would be more readily demonstrated by this method than would damage to white matter. This has been confirmed in practice, for areas of cortical atrophy, superficial tumors and acute cortical injuries have been found to produce well defined and high voltage waves with a frequency of 2 or 3 per second, so that such an uncomplicated cortical lesion can be demonstrated with ease. When there is widespread cortical change there are diffuse but slow potentials of high voltage, and electrodes placed in different areas of the lesion show great independence of activity. On the other hand, in several cases in which the cortex was involved by a deep infiltrating glioma a diffuse area of slow waves of low voltage and inconstant pattern with an indefinite outline was found.

Deep lesions involving "hidden" cortex and white matter, as in a case of a large aneurysm of the internal carotid artery, may cause abnormal waves on both sides of the midline.

In brief, superficial lesions tend to show well localized and easily recognized slow frequencies, while deeper lesions of the same severity are associated with indefinite slow waves of less amplitude, which are spread over an ill defined area. Thus, as Walter originally pointed out, considerable information as to the depth and extent of a lesion can be gained if the type of record obtained, as well as the site of origin and phase relationships of the waves, are studied.

(*c*) Severity of Cerebral Damage: From a study of the 50 cases under review, there appears to be a relationship between the degree of cerebral damage and the disorganization of the normal cortical frequencies. We, in collaboration with E. L. Gibbs,[21] have shown that in conditions of impaired cerebral function there is slowing of the dominant 10 per second frequency, followed by decrease in its voltage. Concurrent with this the voltage of the slower frequencies, which are normally masked by the 10 a second frequency, gradually increases until finally the record is composed entirely of waves with a frequency of 3 per second, which become more persistent and then slow to extinction as deep coma approaches. Such a syndrome can be seen in cases of advanced anoxia. The progressive abnormality is associated with progressive slowing of cortical frequencies and with an increase in voltage of the abnormal waves, which ultimately dominate the picture. This appears to be true also in cases of localized cerebral damage.

In areas of active cortical degeneration, such as those of arteriosclerotic atrophy and the edge of a porencephalic cyst, or in regions where progressive damage is taking place, as around a meningioma, in the edema surrounding an abscess and around a recent cerebral infarct, regular, high voltage waves of from 1 to 3 a second were obtained.

On the other hand, in the cases of infiltrating gliomas the voltages were lower, and in 3 cases of injury to the head of long standing no abnormal waves were found. Presumably, in these cases the damaged cortical cells had undergone complete destruction when the record was taken, and only normal cells remained. In a girl who had had a recent bullet wound in the left occiput, with resulting hemianopia, the left occipital pole was found to be lacerated, and fragments of bullet and bone extended in a wide tract into the lateral horn of the ventricle. After wide cerebral débridement, a clean track was left into the ventricle, and a defect of about 2 to 3 cm. in diameter remained in the occipital pole. Electroencephalograms taken six weeks after the operation did not disclose any abnormally slow activity, presumably owing to complete removal of damaged cortical and subcortical tissue.

It appears, then, that there is a relation between the severity of the electrical disturbance and the degree of cerebral cell damage. Further investigation of this correlation by repeated examination of patients showing clinical change is contemplated.

(*d*) Pathologic Character of the Lesions: The cases in this series in which the lesions were localized included 16 of cerebral tumors—8 of gliomas, 5 of meningiomas and 3 of other tumors—7 of long-standing cerebral traumas, 6 of infections—abscesses and "acute encephalitis"—4 of subdural hematomas; 4 of porencephalic defects; 3 of areas of cortical atrophy; 2 of vascular accidents—1 of sub-

21. Gibbs, F. A.; Williams, D. J., and Gibbs, E. L.: Modification of the Cortical Frequency Spectrum by Changes in Blood Sugar, O_2 and CO_2, to be published.

acute hemorrhage and 1 of a cerebral infarct—and 7 of obstruction of the posterior fossa with resulting high intracranial pressure.

It is apparent, therefore, as Walter and others concluded from similar evidence, that the slow waves emanate from abnormal cortex and not from the causal lesion.

The position of the lesion or lesions having been found, it has already been shown that the size of the abnormal area can be approximately assessed. It may be ascertained that the lesion is superficial or deep. The sharpness of distinction between normal and abnormal tissue appears to be correlated with the sharpness in fall of voltage of the abnormal waves around the disturbance, and from the amplitude and persistence of the abnormally slow waves an estimate of the degree of cerebral damage may be made. Thus, much may be learned about the cerebral lesion in suitable cases. Any one of the criteria mentioned would alone be too indefinite to be of value in the differential diagnosis of the lesion. When all the information is assembled, however, and is correlated with the history and clinical findings, the method may have value in differential diagnosis.

Cases in Which No Electroencephalographic Focus Was Found.—No reference has yet been made to the 41 cases in which no constant focus of slow waves was found. The majority occurred in epileptic patients in whom an underlying gross lesion was suspected; in a few there were signs of intracranial lesion without seizures. In only 7 of these cases were the electroencephalograms normal. In 4 of these patients cerebral tumor was suspected; 1 patient had post-traumatic headache, and 2 had had injuries to the head many years previously. The clinical investigation and subsequent course in these 41 cases have not revealed any further abnormal signs, so that the electroencephalographic diagnosis appears to have been correct. It seems that the abscence of an electroencephalographic focus of abnormal activity can be used as strong evidence against the presence of any supratentorial tumor involving cortex, and the electroencephalogram may probably replace an encephalogram in many of these doubtful cases.

In the remainder of the 41 cases there were cortical potentials characteristic of epilepsy (Gibbs and others[18]). Foci of subclinical or "larval" seizures, but no evidence of a constant focus of the type associated with an organic cortical lesion, were seen. It may be that such foci were masked by the waves of varying voltage and frequency that are characteristic of the record between seizures in epilepsy and that the organic lesions may thus have been overlooked. The differentiation of "organic" and "epileptic" foci appears to be possible in some cases from study of the wave forms recorded, as those from the former are often slower, are maintained in a more regular rhythm and are often almost obscured by the normal frequency, since their voltage is relatively low. This distinction is hazardous, however, and until the different wave spectrums have been investigated by an analyzer, such as that described by Grass and Gibbs,[22] it will be safer to combine the clinical evidences of a lesion with the electrical evidence.

Intracranial Injuries.—In 12 of 26 cases of injury to the head there was a local focus of slow activity, and the cases were therefore included in this series. The lapse of time since the injury varied from five months to twelve years. In all these cases the site of injury had been determined by operation, by a bone defect or by roentgenographic evidence. In each case the abnormal waves were found in the neighborhood of the injury. In 3 cases the records were normal, and in 11 there were widespread abnormal waves characteristic of epilepsy. Instances

22. Grass, A. M., and Gibbs, F. A.: A Fourrier Transform of the Electroencephalogram, J. Neurophysiol. **1**:521, 1938.

of grand mal, petit mal variants and "psychomotor" seizure patterns were seen. Three of the patients showing these types of abnormality had not yet had any seizures. In a small group of cases of acute injury to the head which are not included in this series, the abnormal waves were seen scattered throughout the hemispheres, although they were sometimes maximal around the site of injury. From these cases it seemed that the electroencephalogram would not have the same localizing value for cerebral injury and hematoma as it has with more well defined cerebral lesions.

COMPLICATIONS IN LOCALIZATION

Generalized abnormal cortical frequencies are associated with: (1) high intracranial pressure; (2) unconscious states, including deep sleep, anesthesia and other types of coma; (3) epilepsy; (4) mental disorders, and (5) generalized cerebral degeneration, e. g., Schilder's disease (fig. 6).

Widespread abnormal cortical potentials, if they are not directly related to those arising in a discrete focus, may obscure the focus. The causes of abnormality most likely to hamper the investigator in localizing

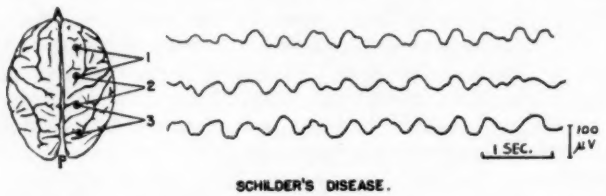


Fig. 6.—Typical records from a case of Schilder's disease. In all 3 such cases studied the electroencephalogram showed high voltage waves of 2 to 3 per second in all leads. This slow activity was more constant and of a higher voltage in the occipital areas, but in no case was there a definite focus.

a cortical lesion are high intracranial pressure, coma and epilepsy. The persistent high voltage slow waves of increased intracranial pressure can be abolished or greatly diminished by intravenous injection of a hypertonic solution of sucrose. During the fifteen to twenty minutes available, repeated electroencephalograms may demonstrate an underlying focus of abnormal waves (fig. 5). This procedure has been used repeatedly in the present investigation, the absence of any focal abnormality indicating the absence of a local supratentorial lesion in the difficult cases of high intracranial pressure without localizing signs.

The presence of epilepsy in association with the organic lesions has already been dealt with.

In the only case in this series in which a focus was overlooked, there was high intracranial pressure with deep coma. The high voltage slow waves from these causes, together with the widespread abnormal waves from the major focus, which was recognized, completely masked the subsidiary focus of abnormality.

COMMENT

Various types and placings of electrodes were used in this investigation. For localizing foci of cortical abnormality, readily movable saline pad electrodes with serial placings on the scalp, as described by Walter, are the most satisfactory. When a truer record of cortical changes in potential is required, as in differentiation of the wave patterns of epilepsy, the use of an indifferent grounded electrode, as described by Tönnies, is desirable. When both these electrode systems were used simultaneously, the rhythmic wave and spike pattern of petit mal epilepsy was repeatedly seen to persist in its true form with single scalp electrodes and an indifferent grounded lead, whereas it was soon distorted and lost its true form in the record from the paired electrodes. On the other hand, waves originating from a localized area were evident with paired electrodes, while generalized frequencies obscured them in the record from single electrodes, because, of course, a change in potential common to each of the paired electrodes causes no difference in potential between the electrodes and so allows a change localized to one of them to stand out clearly.

There did not appear to be any advantage in using the triangulation method advocated by Jasper and Hawke,[23] for similar information is obtained more simply by Walter's technic.

For routine use in a clinic it is probably advisable to begin an investigation with six independent scalp electrodes against a grounded indifferent electrode, thus obtaining as accurate a record of the cortical potentials as possible, and then use a switch box to interconnect the electrodes and a "push-pull" circuit to search for a focus of abnormal waves, if that is thought necessary. With such a procedure, the epilepsies can be differentiated, abnormal waves associated with organic and "functional" diseases investigated and the localization of any focus determined.

As a result of this and other investigations, it appears that organic cortical damage causes progressive slowing of cortical potentials, the predominance of the abnormal waves depending on the severity of the damage. Abnormally fast high voltage activity has been seen only in association with epilepsy, and in only 1 of 64 cases did this persist over the site of cortical damage to a greater degree than elsewhere. The patient in this case had frequent jacksonian fits, and although this fast activity of grand mal type was present, slower frequencies also were present over the lesion. These observations are in contrast to those made by Case and Bucy,[24] who found fast spikes over the lesion

23. Jasper, H. H., and Hawke, W. A.: Electroencephalography: IV. Localization of Seizure Waves in Epilepsy, Arch. Neurol. & Psychiat. **39**:885 (May) 1938.

24. Case, T. J., and Bucy, P. C.: Localization of Cerebral Lesions by Electro-Encephalography, J. Neurophysiol. **1**:245, 1938.

in 3 of their 11 cases. It is important, however, that all their patients had epileptic fits, so that the phenomena they describe may have indicated an epileptic focus associated with the lesion. As an increase in the slower frequencies appears to be characteristic of all cortex undergoing damage, it seems that clinical localization of active cortical lesions can be made with most certainty by using slow rather than fast waves. It has been shown that by observing the position, voltage and phase relationships of these pathologic waves the position of cortical lesions can be determined with a high degree of accuracy and information can also be obtained as to their size, depth and severity. As the method is without risk or discomfort to the patient, its use in experienced hands will prove of great value to clinical neurology.

SUMMARY

The electroencephalogram has been used in the routine investigation of patients in a large neurologic and neurosurgical service over a period of ten months. The site and character of foci of abnormal cortical rhythms were determined in these cases by means of a method of localization described by Walter. In this method the abnormally slow frequencies produced by the damaged cortex in the neighborhood of a lesion are used. Their focus of discharge is determined by studying their relative voltages and phase relationships in three independent and simultaneous records led from the intact skull. The method has been described in detail.

In 105 cases in which intracranial lesions were suspected, there was a close correlation between the actual position of the lesions and that predicted by the electroencephalograms in the 50 cases in which the pathologic process was demonstrated. The characteristics of the electrical discharge were used to deduce the nature of the cerebral lesions in some cases.

In 41 cases in which no cerebral lesion was demonstrated by electroencephalograms subsequent clinical investigation gave negative results.

In the remaining 14 cases the position of predicted cerebral lesions could not be confirmed through lack of clinical and pathologic data.

The value of electroencephalographic examination in cases in which there is a local focus and also in those in which cerebral abnormality is generalized has been considered.

Walter's method has been discussed in relation to other electroencephalographic technics and to the problems encountered in its use.

It is concluded that the method has great practical value as a diagnostic procedure in routine neurologic practice.

NEUROGENIC TUMORS ARISING FROM THE SACRUM

ALFRED W. ADSON, M.D.

FREDERICK P. MOERSCH, M.D.
AND
JAMES W. KERNOHAN, M.D.
ROCHESTER, MINN.

The perplexing problems encountered in the diagnosis and treatment of sacral and anterosacral tumors and cysts have prompted this review of 33 neurogenic tumors. It is usually assumed that neurogenic tumors are found in the cerebrospinal axis or associated with the peripheral nervous system. However, during the last fifteen years we have encountered a number of neurogenic neoplasms associated with the sacrum and independent of the cerebrospinal axis and peripheral nervous system.

The group includes 19 chordomas, 7 ependymomas, 2 ganglioneuromas, 3 neurofibromas, 1 teratoma and 1 spina bifida cystica of the pelvis. It is hoped that a review of the clinical histories, pathologic observations and therapeutic measures employed may offer some assistance in the differential diagnosis and treatment of similar conditions.

Tumors ventral to the sacrum often have been called *Middeldorpf* tumors, but this term should be limited to those teratomatous tumors that arise from the postanal portion of the intestine, formerly described by Middeldorpf. In addition to these and neurogenic tumors, there are such tumors as dermoid cysts, Ewing[1] tumors, teratomas, myelomas, benign foreign body giant cell tumors, fibrosarcomas, chondrosarcomas, fibromas, squamous cell epitheliomas and numerous metastatic lesions (table).

Whittaker and Pemberton[2] stated:

> Located embryonically in the ventral sacrococcygeal region are the spinal cord, nerve tissue, postanal portion of the hindgut, neurenteric canal, caudal end

---

Read at the Sixty-Fourth Annual Meeting of the American Neurological Association, Atlantic City, N. J., May 4, 1938.

From the Sections on Neurologic Surgery (Dr. Adson), Neurology (Dr. Moersch) and Neuropathology (Dr. Kernohan) of the Mayo Clinic.

1. Ewing, J.: Neoplastic Diseases: A Treatise on Tumors, ed. 3, Philadelphia, W. B. Saunders Company, 1928, p. 1035.

2. Whittaker, L. D., and Pemberton, J. deJ.: Tumors Ventral to the Sacrum: A Clinical and Histologic Study, Ann. Surg. **107**:96-106 (Jan.) 1938.

of the notochord and the bony vertebral canal. The embryonic development[3] and subsequent disappearance of the structures in this region aid in explaining the origin of these tumors. The primitive streak lies posterior to the neural groove and arises, as does the neural groove, from the embryonic area. The notochord is formed by the proliferation of cells from the anterior end of the primitive streak. It is epithelial in origin. Early in its development the notochord is surrounded by secondary mesoderm.[4] This, then, becomes the primitive vertebral column. As the vertebral bodies are formed, after the fourth week, the continuity of the notochord is broken. The notochord disappears in the region of the vertebral bodies, but persists in the region of the intervertebral fibrocartilages. After the fourth month the notochord has disappeared as a separate structure, but remnants are believed to persist as the nucleus pulposus of the intervertebral fibrocartilages. Linck and Warstat were of the opinion that rests of chordal cells exist outside the axial skeleton anlage, and these can be recognized in the sacrococcygeal region in the adult. These rests may lie either in the body of the sacral vertebrae or on their anterior or posterior aspects.

Histologically Verified Sacral Tumors

Tumor	Number
Chordoma	19
Ependymoma	7
Neurofibroma	3
Ganglioneuroma	2
Dermoid	12
Teratoma	6
Ewing tumor	5
Benign foreign body giant cell tumor	6 (2 malignant)
Fibrosarcoma	12
Myeloma	3
Miscellaneous	10
Total	85

As the notochord is forming, the primitive groove appears on the surface of the primitive streak. The anterior end of the groove, which is embraced by the posterior portion of the neural fold, deepens and forms a canal between the neural groove and the ventral-lying entodermal vesicle, which is the primitive intestinal canal. This is called the "neurenteric canal" . . ., and it gradually moves to a position caudal to the proctodeum. The neurenteric canal is but a transitory passage and disappears in man before the neural groove closes to form the neural tube.

The postanal gut is formed by the union of the proctodeum and that portion of the hindgut proximal to the neurenteric canal. The proctodeum is a surface depression limited at its depths by the proctodeal membrane. The disappearance of this membrane completes the formation of the rectum and anus. The union of proctodeum and hindgut, however, does not take place at the distal end of the hindgut.[5] That portion of the hindgut distal to the union with the proctodeum

3. Cunningham, D. J.: Textbook of Anatomy, ed. 5, New York, William Wood & Company, 1923, pp. 27-55.

4. Lewis, N. D. C.: A Contribution to the Study of Tumors from the Primitive Notochord, Arch. Int. Med. **28**:434-452 (Oct.) 1921.

5. Middeldorpf, K.: Zur Kenntnis der angebornen Sacralgeschwülste, Virchows Arch. f. path. Anat. **101**:37-44 (July) 1885. Cunningham.[3]

is known as the "postanal gut," and it lies on the ventral surface of the coccyx. . . . This structure atrophies early. It is apparent, therefore, how these primitive structures, as they atrophy, may leave a nidus for further growth, with the formation of a tumor.

PATHOLOGY

Chordomas.—We have included in this series of neoplasms the chordomas, although we are aware that they arise from remnants of the notochord and that their origin is not necessarily ectodermal.[6] On the other hand, these tumors are a group sui generis; they are not epithelial or mesodermal but have some of the characteristics of both epithelium and mesoderm. They are found almost exclusively in two positions in the body, the clivus Blumenbachii and the sacrococcygeal region.[7] In the latter position such a tumor may arise in the sacrum and remain there for the most part; it may grow into the pelvis with the formation of a presacral tumor, or it may grow posteriorly, giving rise to a postsacral tumor. The sites of origin are the notochordal remnants found normally in the nuclei pulposi of the sacrum and possibly heterotopic foci of chordal tissue anterior or posterior to the sacrum. It is interesting that in all the cases of chordoma reported earlier, the growth occurred in the region of the clivus Blumenbachii.

The first case of sacrococcygeal chordoma was observed in 1910 by Feldmann,[8] who removed a presacral tumor the size of an apple from a woman aged 46. This tumor had no definite attachment to the sacrum. Since then numerous reports of such tumors have been made. In our series there were 19 tumors of this type, and 13 of them have been described previously by Fletcher, Woltman and Adson.[9] The characteristics of this type of neoplasm are that the tumor cells tend to grow in islands and frequently in columns (fig. 1). The islands of tumor tissue are surrounded by a varying amount of connective tissue stroma, which varies much in density. The individual tumor cells frequently have a vacuolated cytoplasm and usually are referred to as

6. (*a*) Adson, A. W.; Kernohan, J. W., and Woltman, H. W.: Cranial and Cervical Chordomas: A Clinical and Histologic Study, Arch. Neurol. & Psychiat. **33**:247-261 (Feb.) 1935. (*b*) Cappell, D. F.: Chordoma of the Vertebral Column with Three New Cases, J. Path. & Bact. **31**:797-814 (Oct.) 1928. (*c*) Chesky, V. E.: Sacrococcygeal Chordoma, Arch. Surg. **24**:1061-1067 (June) 1932. (*d*) Joyce, T. M.: Chordoma of the Second and Third Cervical Vertebrae, S. Clin. North America **13**:85-93 (Feb.) 1933.

7. Raven, R. W.: Sacrococcygeal Cysts and Tumors, Brit. J. Surg. **23**: 337-361 (Oct.) 1935.

8. Feldmann, I.: Chordoma ossis sacri, Beitr. z. path. Anat. u. z. allg. Path. **48**:630-634, 1910.

9. Fletcher, E. M.: Sacrococcygeal Chordomas, Thesis, University of Minnesota, 1933. Fletcher, E. M.; Woltman, H. W., and Adson, A. W.: Sacrococcygeal Chordomas: A Clinical and Pathologic Study, Arch. Neurol. & Psychiat. **33**:283-299 (Feb.) 1935.

"physaliferous" cells. The vacuoles contain varying amounts of mucus, but more mucus is present between the columns of tumor cells, where frequently it is found in large amounts. Some of the vacuoles of the physaliferous cells contain glycogen, which can be easily demonstrated with Best's carmine stain for glycogen. However, we have found that even after fixation in a 4 per cent solution of formaldehyde, Best's carmine stain for glycogen gives a positive reaction. This means that all the substances which react to this stain are not glycogen, since glycogen is very soluble in water, and 4 per cent solution of formalde-

Fig. 1.—Section of a chordoma, showing the cells growing in cords with interstitial mucus. Vacuolated (physaliferous) cells are visible. Hematoxylin and eosin; × 170.

hyde is an aqueous solution. In some of our cases we fixed portions of the tissue in dehydrated alcohol and other portions in 4 per cent solution of formaldehyde, and after Best's carmine stain had been applied we compared the reaction and found that the scarlet-staining material was more abundant in the tissue that was fixed in alcohol than it was in that fixed in solution of formaldehyde. We have suggested elsewhere that the substance which gives a positive reaction for glycogen after fixation in solution of formaldehyde be designated by the term

"paraglycogen" or a similar term; we believe it is not true glycogen. The vacuoles of the tumor cells contain mucus, glycogen and paraglycogen, but there are still a few other vacuoles which do not stain for any of these substances or for fat. We have been unable to determine what the content of these remaining vacuoles really is. Sometimes the nuclei of so-called physaliferous cells are vacuolated. The contents of these vacuoles have not been determined.

Cytologically, most chordomas are slowly growing neoplasms, but 2 of this series of 19 were malignant, containing many mitotic figures. In these 2 malignant chordomas the cells were not growing in islands or in columns, as they grow in the more slowly growing types of these tumors. The growths were diffuse and cellular. There were fewer physaliferous cells; also, there were less glycogen, paraglycogen and mucus. Malignant chordomas may metastasize to the lymph nodes, the liver or the lungs. In spite of the fact that most chordomas are slowly growing neoplasms, the ultimate prognosis is not good, because they are rarely encapsulated but invade the bones of the sacrum. Thus total removal is extremely difficult, if not impossible. We have encountered several instances of total removal of an encapsulated chordoma in which the patient was living without recurrence some years later.

Chordoma may occur in the bone of the sacrum, although it is not common in this situation. It occurs more commonly in the hollow of the sacrum and less commonly in its posterior wall. Of the 19 tumors available for study 17 originated in the sacrum, involved it and extended into the pelvis. One tumor developed in the sacrum but did not extend into the pelvis, and 1 developed anterior to the sacrum but did not invade the sacrum.

Ependymomas.—There were 7 ependymomas in this group of sacral tumors, and they were similar to those we have described in other articles (Kernohan and Fletcher-Kernohan) as occurring in the central nervous system. Sacral tumors of this subgroup are interesting because of their close similarity to the other ependymomas we have described (fig. 2). There were 4 of the type we have designated by the term "myxopapillary," because these tumors are a papillomatous type of growth, while the stroma of the various papillae tends to undergo myxomatous degeneration. This degeneration may be so widespread and uniform that a section of the tissue simulates a section of thyroid gland, except that the colloid-like substance stains specifically for mucus and the epithelium-like (or ependymal) cells are on the outside, and not on the inside, of the basement membrane. The ependymal cells in this group of 4 tumors did not contain droplets of mucus. All these tumors were slowly growing.

There was 1 tumor which we have classified as a "cellular variety of ependymoma." This term is somewhat misleading, as it does not designate increased malignancy of the tumor but rather means that the cells of the neoplasm have not formed papillomatous growths or arranged themselves to form canals. This tumor was no more malignant than any of the other tumors of this group. The cellular varieties of ependymoma have a tendency to contain groups of cells that are indistinguishable from those of oligodendrogliomas. We regret that in this instance we were unable to use Hortega's silver carbonate stain for oligodendroglia, since the tissue had been fixed for seven years in 4 per cent solution of formaldehyde. There was 1 tumor that belonged in

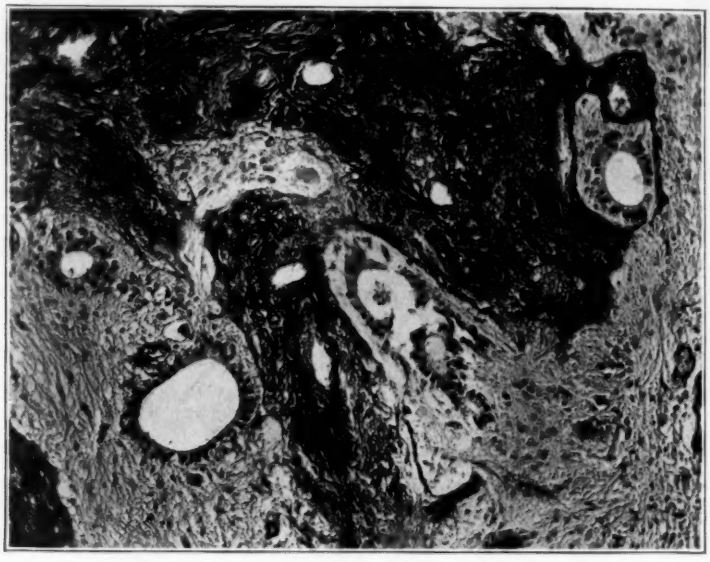


Fig. 2.—Section of an ependymoma from the hollow of the sacrum. Typical ependyma-lined canals surrounded by glial tissue are seen. Glial tissue can be seen invading the bundles of connective tissue. Van Gieson stain; × 105.

parts to the cellular type and in other parts had ependyma-lined canals. This is the type of tumor generally recognized throughout the literature as an ependymoma; therefore, further description is unnecessary. Finally, there was 1 tumor that contained all three types of ependymoma; namely, parts of it were myxopapillary, parts had a cellular arrangement and there were some ependyma-lined canals similar to those seen in the central canals of spinal cords of children.

It was a study of the mixed types of ependymoma that enabled us to distinguish the three subtypes of this tumor. The subdivision may be only of academic interest, but by making it we have been enabled to include among the ependymomas tumors that previously had been

classified with other varieties of gliomas. This is of importance because, as a whole, ependymomas are extremely slowly growing neoplasms which frequently can be completely enucleated, and an excellent prognosis can be given.

Ganglioneuromas.—There were 2 examples of this type of neoplasm. One of the growths was in the bones of the sacrum, extended into the hollow of this structure and protruded posterior to the sacrum. It was a firm, almost fibrous growth with a definite capsule and had produced a large defect in the bone. Histologically, it was a typical ganglioneuroma (fig. 3) with numerous large multipolar nerve cells which had large vesicular nuclei and prominent centrally situated nucleoli. Nissl granules were seen to be numerous when the cresyl violet stain was used, whereas the modified silver impregnation method for nerve cells revealed numerous branching dendrites, excellent axis-cylinders and intracellular nerve fibrils. The cells were similar to sympathetic nerve cells, except that they were surrounded by neither endocapsular nor ectocapsular cells. Usually the cells were collected into large clumps, and there were as many as fifteen or twenty nerve cells in one group. Some of these cells had become fixed, so that multinucleated ganglion cells were fairly common. There were some nerve cells with vacuoles which varied in size; some of the cells were markedly distorted by the size of the vacuoles, so much so that the cells had almost been destroyed. This vacuolar degeneration of nerve cells in ganglioneuromas, especially of those cells arising from the sympathetic nervous system, was so common as to be almost characteristic of this type of neoplasm.

The second tumor belonging to this group occurred in a child; a large mass almost filled the pelvis and arose from the hollow of the sacrum. It was impossible to remove this mass, and only biopsy was performed. The histologic appearance of the tumor was almost identical with that described previously. However, there was a history of marked increase in symptoms during the last few months before the child was brought to the clinic, and it is possible that some other portion of the tumor was more rapidly growing or even highly malignant; in that case the tumor could have been a neuroblastoma. However, the portion of tissue removed for biopsy was a typical ganglioneuroma.

The stroma of both of these tumors was made up of connective tissue, through which nerve fibers ran, sometimes as single fibers and sometimes as large bundles. No myelin sheaths surrounded the axis-cylinders, and we were unable to determine where they went or the nature of their termination.

Neurofibromas.—There were 3 neurofibromas; 2 were in the hollow of the sacrum and 1 was posterior to the sacrum. The latter neoplasm

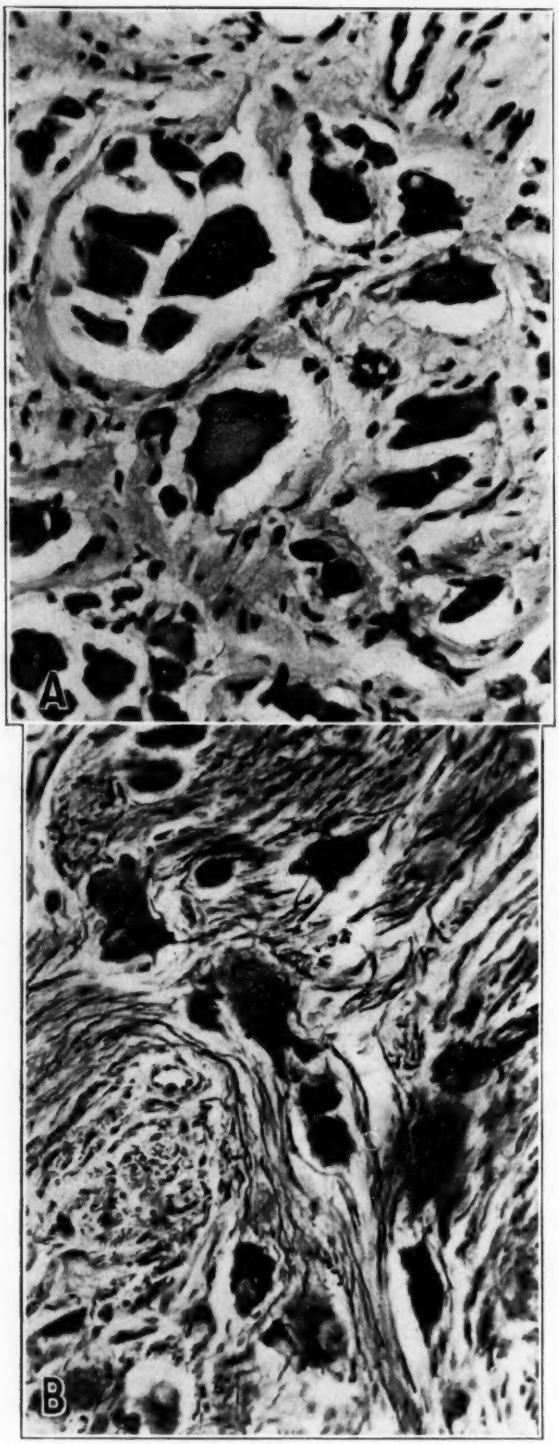


Fig. 3.—*A*, section of a ganglioneuroma. The cells tend to grow in groups or islands and vary much in size. Nissl bodies can be seen in the cells. Some cells are degenerating. There are no capsular cells. Cresyl violet stain; × 275. *B*, section of a ganglioneuroma impregnated with silver nitrate; × 255. The nerve cells have many dendrites, and axis-cylinders are seen in large numbers in the stroma.

was associated with spina bifida occulta, and the neoplasm was diffuse and extended into the corium. It was not highly malignant but had widely infiltrated the subcutaneous tissues and was growing down to the periosteum. Histologically, it contained numerous fibrils arranged in a manner similar to that in which the fibrils in Meissner's tactile corpuscles are arranged. The cells and fibrils did not stain specifically by Ramón-Cajal's gold chloride and sublimate method or by Hortega's silver carbonate method. The fibrils, moreover, did not have any affinity for the fuchsin of Van Gieson's stain, and although they did stain with Mallory's phosphotungstic acid hematoxylin, the tinctorial reaction was not specific for either connective tissue or neuroglia. The tumor was widely resected and was found not to be attached to, or associated with, the sac of the spina bifida. The other 2 tumors were typical neurofibromas with interlacing fibrils, foam or fat-containing cells and spindle-shaped nuclei; however, palisading of the nuclei was not a prominent feature, although there was an attempt at palisading in places. There was some blood pigment, and there were areas of degeneration and some lymphocytes in each. As far as we could determine, each of the 3 neoplasms was solitary and was not a part of the manifestations of Recklinghausen's disease.

Teratomas.—One neoplasm in the hollow of the sacrum has been classified as a teratoma although we did not observe all the elements necessary to allow accurate classification in that group. Glia cells in the cerebral and cerebellar cortex were intermingled with connective tissue, but there were no other mesodermal, ectodermal or entodermal elements. The mass was not large; it had not been growing, and we did not see any signs of growth, as the tissue was adult brain tissue. The cerebral cortex contained a pyramidal type of nerve cells with axis-cylinders, and astrocytes were present, but we were unable positively to identify oligodendroglia or microglia, and we could not see myelin sheaths. The cerebellar cortex contained both the molecular and the granular layer, but no Purkinje cells. The neoplasm was in the retroperitoneal tissue, in the hollow of the sacrum, and was not a part of an ovarian teratoma.

Comment.—There have not been many studies on neurogenic tumors of the sacrum, from the pathologic, the diagnostic or the therapeutic point of view. During early embryonic life the spinal cord is equal in length to the spinal column; it even curves around the caudal end of the spine and is attached to the inner aspect of the coccyx. Since the vertebral column grows at a greater rate than the spinal cord, the caudal end of the latter becomes stretched and attenuated, but remnants of neurogenic tissue remain behind along the course of the original spinal medulla. The small terminal portion anterior to the coccyx usually is referred to as the sacrococcygeal body. It is from such a remnant that

a neurogenic neoplasm can develop, either anterior or posterior to the sacrum, but it is more difficult to understand how a neurogenic tumor can occur within the bones of the sacrum.

In the entire group of tumors of the sacrum encountered at the Mayo Clinic, non-neurogenic as well as neurogenic, the greatest number, 27.5 per cent, have been chordomas. This type of tumor has received much attention in the literature; more than 200 cases have been described and in more than 50 per cent the growth has been found in the hollow of the sacrum. The histologic appearance of chordoma is characteristic, and we were chiefly interested in the contents of the vacuoles in the physaliferous cells.

Our attempts to identify the contained material and our difficulties therein have been recounted in the foregoing paragraphs. We have been unable to determine from our own experience the tissues to which these neoplasms metastasize or the effect of roentgen therapy on their cytologic picture or ultimate course. In cases in which growth is slower the neoplasm sometimes widely invades the bone, so that, in spite of the fact that the immediate prognosis is good, there is little hope of complete cure, and the ultimate prognosis is not good. A small number of these tumors are encapsulated, and when a capsule is present, complete enucleation can be easily carried out; for these the prognosis is excellent.

The filum terminale has been shown by Harmeier to contain cells similar to those seen elsewhere in the central nervous system, and neoplasms which arise from the filum terminale are of the same general nature as those found in the spinal cord or brain, except that there is a greater percentage of ependymomas among the tumors which arise from the central nervous system (Adson, Kernohan and Woltman [6a]). We have described 7 ependymomas of the sacrum. The other varieties of glioma might be represented by 1 tumor in which we observed cerebral and cerebellar cortical tissue although there was no evidence of progression of the tumor; there were also 2 ganglioneuromas. The ependymomas were similar to those that have been described elsewhere in the nervous system (Kernohan and Fletcher-Kernohan). All these tumors were slowly growing, were encapsulated and had destroyed the bone by pressure and not by direct invasion. Four of the 8 growths were of the myxopapillary type; in these we observed an abundance of mucus in the degenerated stroma of the papillary projections. We did not see any mucus in the cytoplasm of the cells. There were 2 ependymomas of the cellular variety in which we saw several ependyma-lined canals, and the seventh tumor was of the so-called epithelial type. This last tumor had numerous ependyma-lined spaces or canals, which seemed to be empty; the lining cells were not ciliated.

The tumor which contained cerebral and cerebellar cortical tissue showed no signs of growth. We feel that this tumor represented a

heterotopic mass, in spite of its size, although it possibly represented a teratomatous type of growth from which some of the elements necessary for its classification as typical teratoma were missing. The 2 ganglioneuromas were excellent and typical examples of this type of neoplasm. The cells contained all the elements of normal adult nerve cells, and many cells had two or more nuclei. Some cells were fused, and others were undergoing a cystic type of degeneration. The cells were typical sympathetic nerve cells, except that there were neither ectocapsular nor endocapsular cells. These tumors have been found in all parts of the body where sympathetic ganglia are normally situated. Little need be said about the neurofibromas. They were fairly typical examples of this type of neoplasm except that they were more cellular and more actively growing than the average tumor belonging to this class; neither patient with neurofibroma had any stigmas of Recklinghausen's disease.

SYMPTOMATOLOGY

The symptoms produced by tumors originating within the sacrum and extending into the pelvis, or originating anterior to the sacrum and subsequently eroding the sacrum, are similar, irrespective of the cytologic structure of the tumors. Local pain and tenderness are present in most instances. Tumors that originate within the sacrum cause a greater degree of pain than those that originate anterior to the sacrum. As the tumors increase in size and fill the pelvis they frequently produce constipation and urinary retention, because of involvement of the sacral nerves. The tumors that extend cephalad into the lumbar canal produce pain that extends into the buttocks and down one or both legs, with accompanying saddle anesthesia and loss of the achilles and the anal reflex. Occasionally a tumor that extends dorsally to the sacrum will grow to such size that the patient is able to palpate the mass.

From a review of the cases of chordoma, it is apparent that the tumors afflict males twice as often as they afflict females. They also occur at a later age than do the ependymomas, ganglioneuromas, dermoids and teratomas. In our series of cases of this type of tumor 1 developed in a patient who was 3 months of age. The remainder of the tumors originated in the third, fourth or fifth decade of life, with the exception of 4, of which the symptoms developed when the patient had passed 60 years of age. Trauma appears to be a factor in producing the symptoms. The average duration of symptoms prior to admission at the Mayo Clinic was thirteen months. A third of the patients complained of pain extending down the legs. Two thirds complained of pain in the perineum and sacrum. Sensory changes were present in a third of the cases. In about half there was urinary retention, and incontinence

occurred in 5 of the 19 cases. Cystitis was present in but 2 cases. The tumors varied in size from that of a tennis ball to that of a man's head. Routine laboratory studies showed no abnormality except for the cystitis.

The two most important examinations in cases of chordoma are digital examination of the sacrum through the rectum and roentgen examination of the pelvic bones.[10] In many instances it is possible to palpate irregular masses that have eroded through the sacrum on the dorsal surface. Rectal examination revealed the presence of a mass in the hollow of the sacrum in 18 of the 19 cases. These masses were situated posterior to the rectum. They were densely adherent to the sacrum. They were irregular and frequently nodular, but not cystic.

Fig. 4.—Destruction of sacrum by a chordoma.

In a number of instances the mass displaced the rectum anteriorly and extended upward in the pelvis to the upper level of the sacrum.

Roentgen findings in the presence of chordoma were almost pathognomonic (fig. 4). Camp,[11] of the Section on Roentgenology at the Mayo Clinic, has described the chordomatous lesions as expanding growths. The lateral view revealed destruction of the sacral body in all directions. The tumor eroded the bone dorsally to include the sacral canal and eroded it ventrally to allow the tumor to fill the pelvis. The

10. Hundling, H. W.: Ventral Tumors of the Sacrum, Surg., Gynec. & Obst. **38**:518-533 (April) 1924.

11. Camp, J. D.: The Roentgenologic Localization of Tumors Affecting the Spinal Cord, Am. J. Roentgenol. **40**:540-544 (Oct.) 1938.

anteroposterior view revealed the same findings, with the exception that ridges of bone and spicules still persisted between the islands of tumor that had broken out of the sacrum. In a few instances, when lumbar invasion has been suspected, studies made with iodized poppyseed oil have proved of value in determining the upper level of the growth in the lumbar canal.[12]

Studies of spinal fluid were made in only 1 of this series of cases of chordoma, a case in which they showed abnormality.

Fig. 5.—Erosion of the sacrum and lumbar vertebrae by pressure from an ependymoma.

The symptoms produced by ependymoma originating from the filum terminale are similar to those produced by sacrococcygeal chordoma. With the exception of 2, which occurred, respectively, at 2½ years and 44, ependymomas occurred in the second and third decades of life.

12. Ribbert, H.: Ueber die Ecchondrosis physalifora sphenooccipitalis, Centralbl. f. allg. Path. u. path. Anat. **5**:457-468, 1894; Ueber die experimentelle Erzeugung einer Ecchondrosis physalifora, Verhandl. d. Cong. f. inn. Med. **13**: 455-464, 1895.

Males were more prone to have these tumors than females, as was true, also, of chordoma. Urinary retention with incontinence, associated with pain extending into the buttocks and legs, occurred more often among patients with ependymoma than among those with chordoma. Saddle anesthesia and loss of achilles and anal reflexes were frequent accompanying symptoms of ependymoma. The duration of symptoms prior to admission of the patients averaged six and a half years, a period approximately five years longer than that in cases of chordoma.

Fig. 6.—Neurofibroma of the lumbosacral canal, producing definite bony absorption of the fifth lumbar and first and second sacral segments.

The masses detected on rectal examination were much smaller, as a group, than were the chordomas. In 3 instances the ependymoma filled the lumbar canal, in addition to eroding the sacrum. The roentgen features, as described by Camp, are characteristic, in that the destruction of bone was the result of erosion (fig. 5) from pressure, rather than from invasion as in cases of chordoma. The erosion from pressure enlarged the sacral canal. Usually the erosion extended upward into the lumbar canal in such a manner as to produce partial absorption of the

lumbar peduncles and laminas. Puncture in the fourth lumbar space resulted invariably either in a dry tap or in the obtaining of bloody fluid. Studies with iodized poppyseed oil proved effective in determining the upper level of the lumbar extension, providing the substance was introduced about the tumor.

One ganglioneuroma occurred in a girl 5 years of age. Constipation and lumbar pain were the chief complaints. All the tumors were large, averaging about the size of a grapefruit. The ganglioneu-

Fig. 7.—Erosion from pressure by extensive dermoid of the pelvis.

romas were situated in the hollow of the sacrum, and the roentgen examination showed no abnormality. The neurofibroma just mentioned was situated over the lumbosacral area extending from the fourth lumbar to the second sacral segment and was accompanied with a bifid defect of the lumbar portion of the spine (figs. 6 and 7).

Spina bifida cystica of the pelvis occurs rarely.[13] However, in July 1936 a woman 22 years of age came to the Mayo Clinic complaining

13. Adson, A. W.: Spina Bifida Cystica of the Pelvis: Diagnosis and Surgical Treatment, Minnesota Med. **21**:468 (July) 1938.

of pain in the region of the sacrum, present off and on since she was 13 years of age. At times the pain extended along the posterior aspect of the left leg. Subjective numbness in the saddle area was present, but this was not demonstrated objectively. The woman complained of occasional urinary retention, and she had been told that she had had cystitis with episodes of pyelonephritis. During the episodes of pyelonephritis she had been compelled to rest in bed and to undergo treatment. She stated that she had been subjected to laparotomy for a pelvic tumor. Exploration had revealed a doughy mass in the hollow of the sacrum, said to have been about the size of a grapefruit. It was situated posterior to the rectum and had been left undisturbed during the laparotomy. The general examination performed by us showed no abnormality except a tumor in the hollow of the sacrum. It was associated with anomalous development of the sacrum and coccyx. Although roentgen evidence of anomalous development was present, there was no evidence of true erosion or invasion of bone. Rectal examination revealed the presence of a doughy mass, which gave the suggestion of fluctuation and was situated in the hollow of the sacrum. The consistency of the tumor and the roentgen evidence suggested the possibility of spina bifida cystica of the pelvis. Surgical operation was advised and accepted. The details of the findings and the operative procedure will be presented in the next section.

SURGICAL TREATMENT

Chordomas [14] do not lend themselves to complete removal, since they both erode and invade the bony tissues of the sacrum. However, of our 19 cases we were able to carry out extensive and radical removal in 10. This was accomplished by approaching the tumor from the dorsal surface of the sacrum or by resecting the coccyx through a Kraske incision to uncover the tumor in the hollow of the sacrum. In the remaining cases of the group less formidable operations were employed, and resort was had to irradiation. All tissue was examined by one of us (Kernohan). In 9 cases several courses of high voltage roentgen therapy were employed. Although radical and complete removal is impossible, it appears from a review of our cases that surgical treatment and irradiation are valuable in ameliorating the pain and in prolonging life, although they were not materially effective in relieving the neurologic symptoms of vesical and rectal retention and incontinence nor did they relieve the sensory loss in the saddle area. There

14. Stewart, M. J.: Malignant Sacrococcygeal Chordoma, J. Path. & Bact. **25**:40-62 (Jan.) 1922. Stewart, M. J., and Morin, J. E.: Chordoma: A Review, with Report of a New Sacrococcygeal Case, J. Path. & Bact. **29**:41-60 (Jan.) 1926.

were no surgical deaths in the group. Fourteen patients lived one year or more; 10 patients lived three years or more; 4 patients lived five years or more; 1 lived nine years, and another, who was operated on approximately thirteen years ago, is still living at the time of this report. Twelve patients obtained worth while results, to the extent that they were free from pain and were able to return to work until recurrent symptoms appeared.

The ependymomas lend themselves to much more satisfactory surgical treatment than do the chordomas, since they do not invade the bone. It is true that they erode the bone by pressure and manage to fill every crevice and foramen with tumorous tissue. The tumors usually are encapsulated and often stretch the arachnoid and dura in such a manner that the meninges form numerous pockets along the intervertebral and sacral foramens. When the tumor extends upward into the lumbar region, it is found closely adherent to the fibers of the cauda equina.[15] The tumor itself is friable and rather vascular and cannot be lifted out as easily as can a meningioma or a neurofibroma. After the tumor has been uncovered by extensive laminectomy, removal becomes a tedious affair and requires patience and perseverance on the part of the surgeon.

There were 2 deaths in this series of cases of ependymoma. One of the patients who died was a child 2½ months of age, on whom cecostomy was performed for intestinal obstruction but no attempt was made to remove the tumor; a specimen of the tumor was removed for biopsy. The second death occurred four days after operation and was the result of surgical shock arising from the extensiveness of the operation. This suggests that if the tumor involves the sacrum and the lumbar canal, the operation should be divided into two stages. In 1 or 2 cases removal was incomplete but with the aid of diagnostic study of fresh tissue the surgeon in the future should obtain better results than have been obtained in the past. Three of the patients have survived twenty-five, thirteen and eight years, respectively; the others have lived for shorter intervals but are still living at the time of this report. The surgical results from removal of ependymoma are materially better than those following operation for chordoma. Recurrences will take place unless all of the tumor is removed. Our patient who has survived eight years is complaining of return of his pain at the time of writing. Two of the patients continued to have vesical incontinence and saddle anesthesia, but neither of these symptoms prevented resumption of regular work.

---

15. Woltman, H. W.; Kernohan, J. W., and Adson, A. W.: Gliomas of the Region of the Cauda Equina, Proc. Staff Meet., Mayo Clin. **4**:391-393 (July 6) 1932.

In the 2 cases of ganglioneuroma recurrence developed, respectively, thirteen months and seven years after biopsy and irradiation. The patient mentioned before who had an extensive neurofibroma underwent extensive resection of the tumor in two stages, with the addition of four courses of high voltage roentgen therapy. He has survived eight years at the time of this report and has lived a useful life, although he has been troubled with a moderate amount of pain.

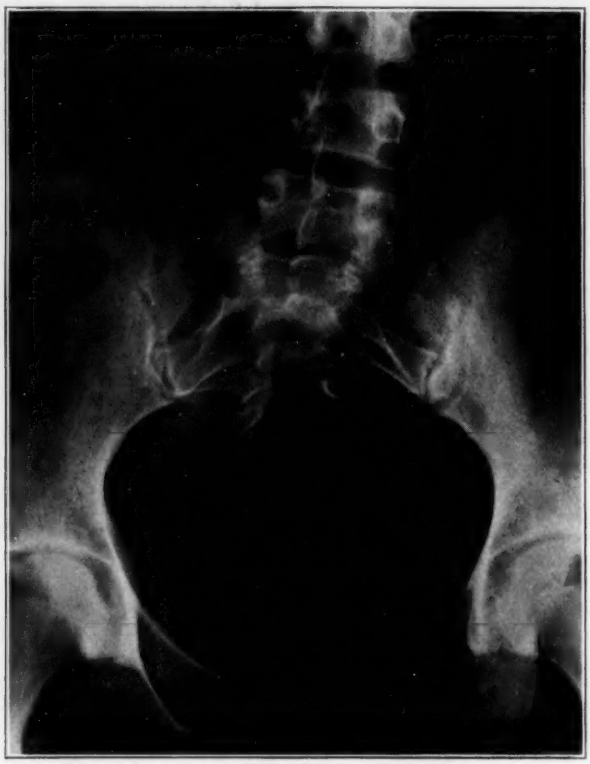


Fig. 8.—Malformation of the sacrum caused by spina bifida cystica that originated in the sacral region and extended into the pelvis.

In the case of spina bifida cystica laminectomy was performed opposite the third and fourth segments of the sacrum, through an incision at the midline of the dorsum. When the dural sac was exposed, it was found to communicate with the pelvic mass (figs. 8 and 9). The sac was opened at the lower end of the incision, and the cerebrospinal fluid in the subarachnoid space was found to communicate with the fluid within the pelvic mass. It then was necessary to determine whether the sac contained nerve elements, and it was found that the only struc-

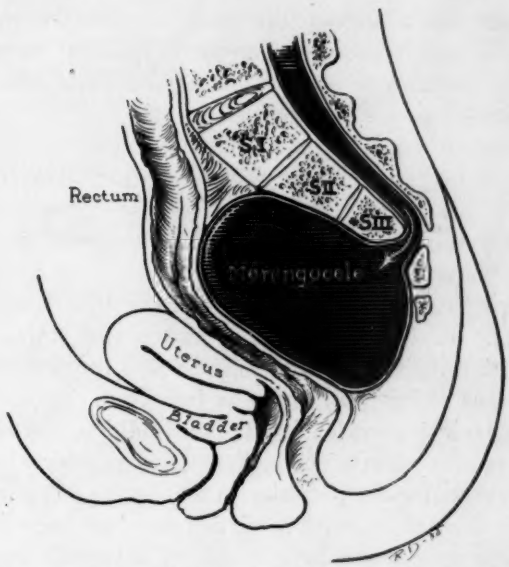


Fig. 9.—Schematic illustration of spina bifida cystica situated in the pelvis, posterior to the rectum, and in the retroperitoneal space. *SI, SII* and *SIII* designate the first, second and third sacral segments of the spine.

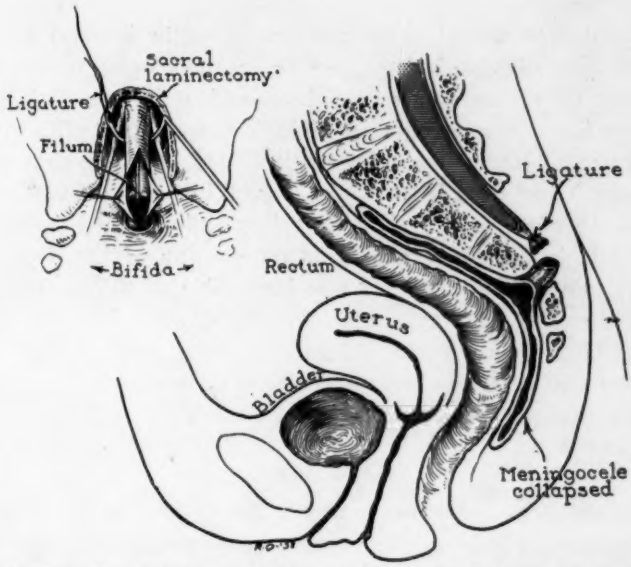


Fig. 10.—Drawing showing exposure of the caudal end of the sac through a small laminectomy wound and resection and closure of the sac, permitting the pelvic spina bifida cystica to drain into the soft tissues and to collapse.

ture that passed down through the dural sac into the pelvis was the filum terminale, which measured about 2 mm. in diameter. There were no nerve elements in the sac at this situation. The nerve fibers had left the dural sac at a higher level.

The problem that confronted one of us (Adson) was how to remove this sac; it soon became apparent that it was impracticable to attempt removal of the pelvic mass. Therefore it was decided to divide and ligate the dural tube (fig. 10) in the sacral canal, thus closing the caudal end. This was accomplished with purse-string suture and additional reenforcing ligatures. Exploration of the pelvic mass showed that a catheter could be introduced for 5 inches (13 cm.). Subsequent exploration with a lighted retractor showed that the arachnoid lining of the dural sac was rather gray and was free from any unusual masses. This seemed convincing evidence that the condition was not a dermoid but was spina bifida cystica which had extended anteriorly into the pelvis, in the retroperitoneal space posterior to the rectum. After the cerebrospinal fluid in the pelvic portion of this sac had been aspirated, the walls were seen to collapse as a result of increased intra-abdominal pressure. Thus, it seemed that if the distal portion of this sac was left open it would automatically collapse and the wall become adherent. This was done, and the sac was left undisturbed. The wound was closed and the patient cared for much as other patients who have spina bifida are treated.

The patient remained under observation in the hospital for sixteen days and was dismissed from the clinic twenty-one days after the operation. It was necessary to catheterize her for the first five days after operation. Postoperative neurologic examination did not furnish any additional information. The patient said that the pain was less severe than it had been but that she was still conscious of some paresthesia on the outer aspect of the left foot and around the saddle area of her buttock. Rectal examination on the day of her dismissal did not reveal any pelvic mass. It was impossible to palpate any sort of fulness; therefore, it was apparent that the mass had become thoroughly collapsed and had been kept so by the pelvic organs and the intra-abdominal pressure. In a recent letter the patient stated that she was feeling normal and had returned to work.

SUMMARY

Chordoma as a rule occurs in middle life or later while ependymoma occurs before middle life. The onset of symptoms of chordoma is much more rapid than is that of ependymoma. Chordoma expands the sacrum by erosion and invasion, while ependymoma enlarges the sacrolumbar canal by erosion from pressure. Chordoma grows rapidly while ependymoma grows slowly. The former lends itself poorly to surgical removal.

while the latter is amenable to surgical treatment. Irradiation is moderately effective in retarding growth of both tumors. Extensive resection combined with irradiation in the treatment of chordoma offers palliation of pain but little or no relief of vesical, rectal or sensory and reflex disturbances. Radical removal of ependymoma will effect cure as far as survival is concerned but offers little or no relief of vesical, rectal, sensory and reflex disturbances. Removal of ependymoma requires patience and persistence and gentle handling of nerve roots. If results are to be accomplished in the treatment of ganglioneuroma and neurofibroma, early recognition and radical removal are necessary. Spina bifida cystica of the meningeal type can be repaired by simple ligation of the meningeal canal, without removal of the cystic mass from within the pelvis.

LOCALIZED NONSUPPURATIVE ENCEPHALITIS ADJACENT TO A FOCUS OF INFECTION IN THE SKULL

MILES ATKINSON, M.D., F.R.C.S. (ENG.)
NEW YORK

Localized nonsuppurative encephalitis has not as yet been generally recognized by neurologists, neurosurgeons or otologists, yet it arises more frequently than the sporadic accounts of cases in the literature would lead one to expect and is of considerable clinical importance. Characteristically it presents the signs of an abscess, but no abscess is found on exploration of the brain, and the patient in most cases recovers.

Occasionally he dies and there is discovered at autopsy an area of hemorrhagic encephalitis without suppuration. The first case was described by Oppenheim [1] in 1899, and since then others have been reported by Voss (F.);[2] by Borries,[3] who spoke neatly of "the syndrome of abscess without abscess," and by Adson,[4] Symonds,[5] Voss (O.) [6] and others. In all the recorded cases, with 3 exceptions, the lesion has occurred in the temporal lobe as a result of infection in the ear, and it is generally held that diagnosis is impossible except by the negative results of brain puncture. It is the object of this paper to show that localized encephalitis without suppuration occurs in the same situations and from the same causes (except for metastasis) as an abscess, though less often; to discuss the pathology, and to paint a clinical picture which will allow the recognition of this condition in most instances without an exploratory operation.

Based on a paper read at a meeting of the New York Neurological Society, Dec. 7, 1937. The discussion appears in the transactions of the society published in the May 1938 issue of the ARCHIVES.

1. Oppenheim, H.: Zur Encephalitis acuta nonpurulenta, Berl. klin. Wchnschr. **37**:201 (March 5) 1900.

2. Voss, F.: Encephalitis haemorrhagica und Schläfenläppenabszess nach Otitis media, Ztschr. f. Ohrenh. **41**:323, 1910.

3. Borries, G. V. T.: Encéphalite otogène hémorragiqiue, Rev. de laryng. **53**:49 (Jan.) 1932.

4. Adson, A. W.: Three Cases of Pseudo-Brain Abscess, S. Clin. North America **4**:503 (April) 1924.

5. Symonds, C. P.: Some Points in the Diagnosis and Localisation of Brain Abscess, J. Laryng. **42**:446 (July) 1927.

6. Voss, O.: Otitis media und Encephalitis, Ztschr. f. Hals-, Nasen- u. Ohrenh. **21**:596 (May 10) 1928.

PATHOGENESIS

Oppenheim maintained that the association of the encephalitis with the condition in the ear was fortuitous, but all subsequent observers have agreed that the two are causally related, the encephalitis being a direct consequence of the aural infection and in the nature of an abortive abscess. If that view is correct, localized nonsuppurative encephalitis should occur in the same situations and under the same conditions as an abscess. It should be found not only in the temporal lobe but also in the cerebellum, with frontal sinusitis as well as with otitis media, and after open fractures of the skull. It is. Of the 3 cases reported in the literature in which there were exceptions to the temporal site, the process in 1 was situated in the cerebellum and was of otitic origin (Behlau [7]) and in 2 was in the frontal lobe and a result of sinusitis (Richardson [8]).

The present paper completes the picture. It is based on 11 cases of this type, some of the patients being under my care and others in the care of colleagues, who have discussed the cases with me and have allowed me to observe and report them here.[9] In 8 of the 11 cases the condition occurred in the temporal lobe and in 1 in the cerebellum after infections of the ear; in 1 in the frontal lobe after a fracture of the skull involving the frontal sinus, and in 1, in the parietal lobe after an open fracture with infection of the wound. This series, then, includes all parts of the brain in which abscesses tend to occur and all conditions producing them except sinusitis, for which reliance must be placed on Richardson's 2 reported cases.

PATHOLOGY

It has been shown that localized encephalitis appears in the same places and under the same circumstances as an abscess. Presumably the path of infection is the same. At least, the infection passes from a focus in skull or scalp to the brain substance, passing, though this has not yet been proved, along the same route as that which I [9a] have shown is taken in cases of abscess. Localized encephalitis is, in fact,

---

7. Behlau, C.: Statistische Mitteilungen über die in den Jahren 1920-1926 an der Heidelberger Klinik beobachteten otogenen Hirnkomplikationen, Ztschr. f. Hals-, Nasen- u. Ohrenh. **21**:26 (May 10) 1928.

8. Richardson, D. Y.: Jacksonian Attacks in Connection with Extradural Abscess of the Frontal Lobe, Brit. M. J. **2**:1101 (Dec. 15) 1934.

9. Drs. John R. Page, James G. Dwyer, Marvin F. Jones and A. S. Wilson granted me permission to study patients in the Manhattan Eye, Ear and Throat Hospital, and Dr. Foster Kennedy allowed me to observe a private patient.

9a. Atkinson, M.: Hunterian Lecture on Abscess of the Brain: Its Pathology, Diagnosis and Treatment, Lancet **1**:483 (March 10) 1928.

merely one stage in the process of local infection of the brain from an adjacent focus. Infection anywhere in the body behaves in the same general way. It may subside without suppuration, or it may form an abscess, or it may be so virulent and spread so rapidly that there is no time for pus to form. So in the brain there are the three varieties of localized infection: (1) simple infective encephalitis which is an abortive abscess; (2) suppurative encephalitis or abscess; (3) acute hemorrhagic encephalitis.

Simple Infective Encephalitis.—No accurate pathologic description of this variety can be given, because one of the conditions of placing a case in this group is the recovery of the patient. The process, therefore, can only be guessed at by analogy. One presumes an area of encephalitis such as that which is observed surrounding an abscess, but which has failed to suppurate owing to the relatively benign character of the infection. This encephalitis is sufficiently severe and widespread to produce focal signs, but gradually resolves. It is truly an abortive abscess. In this group belong cases such as those described by Adson and Symonds—in fact, the majority of cases reported in the literature.

Acute Hemorrhagic Encephalitis.—This group is distinct from the preceding one in pathologic features and clinical course. It is a much more acute infection, which can be fatal; for which reason something is known of the postmortem appearances.

Macroscopically, in the one case in which I had the opportunity to examine the brain, section showed an indefinitely demarcated area of red softening extending inward to the lateral ventricle. In two places in this area were patches of necrosis, but no suggestion of a pyogenic membrane or of true abscess formation. Similar appearances have been recorded by Behlau, Borries and Esch.[10] In these cases the condition is usually labeled "acute abscess." I have fallen into this error in the past, misled by the breaking-down areas which in fact are due not to suppuration but to the virulence of the infection causing tissue necrosis.

Microscopically, the area contained scattered areas of hemorrhage, mostly perivascular; there were marked lymphocytic perivasculitis and diffuse infiltration of degenerating brain tissue with inflammatory cells.

The responsible organism I do not know, as a culture which was taken proved to be contaminated and I am not aware of any report on this aspect by other observers. I suspect that it is different from that in the preceding group, which is due to a pyogenic organism, partly because of the similarity in the microscopic appearance in this case and

10. Esch, A.: Embolischer Erweichungsherd oder otogener Hirnabscess im Linken Schläfenlappen? Klin. Wchnschr. **1**:781 (April 15) 1922.

that in cases of encephalitis due to virus infections, partly because of the hemorrhagic character of the lesion and its association with a similar primary complaint—in 4 of 8 cases in this group the disease followed an acute infection of the upper respiratory tract, 2 cases occurring in the course of an epidemic of influenza.

Serous Encephalitis.—A third variety of encephalitis is distinguished from the infective type by the clinical picture and course. In these cases there are signs of focal involvement of the brain which disappear within twenty-four hours or so after draining the primary focus, a fact which suggests that they are due to cerebral edema. I have therefore called the condition "serous encephalitis." Because the patients recover, the pathologic process is again conjectural, but it is presumably akin to the effusion into a joint from a periarticular infection. Infection reaches the dura from the local focus, causes pachymeningitis and thus localized serous leptomeningitis—the *méningite de voisinage* of the French writers. With this there is always some degree of edema of the adjacent brain, what might be called *encéphalite de voisinage,* but usually no more than enough to cause the localized headache. Sometimes, however, edema is more extensive and produces focal signs which can be, and often are, mistaken for an abscess. Always there is an undrained or inadequately drained suppurating focus immediately adjacent, and in 3 out of 5 cases of my own, and in the case reported by Richardson, there was an extradural abscess. Encephalitis of this sort, if unrelieved, can change to the infective variety (Richardson's case 2), or an abscess may develop. I suspect that many cases of abscess which start with convulsions are in the first place examples of this condition with an unrelieved dural or extradural focus, prompt treatment of which might prevent formation of the abscess.

SYMPTOMATOLOGY

I. *Simple Infective Encephalitis.*—Most of the reports in the literature refer to cases in this group, and Symonds has said with much truth that such cases present no characteristic clinical picture. The physical signs are those of a focal lesion in a region of the brain adjacent to a focus in the skull, and the presence of such a focus promptly suggests an abscess. Thought is still in terms of the result rather than of the process. Once clinicians begin to think, in regard to the brain as with other organs, in terms of the whole course of the inflammatory process, half the difficulty will be gone. It is a question of conditioning, or rather of reconditioning, a reflex. There are two observations which help to decide the diagnosis. The first is the cell count of the spinal fluid, which is often high—in hundreds in cases of encephalitis, as compared with tens in cases of abscess—with mainly

polymorphonuclears. In very low grade infections, as in the case to be described, there may be no increase in cells, but this finding is also against the presence of an abscess. The second is the "association syndrome." Borries pointed out the importance in diagnosis of an abscess of lessening of the severity of the spinal fluid picture at the same time that the focal cerebral signs are increasing, the "dissociation syndrome." In the cases under consideration, signs presented by fluid and brain keep step with each other, increasing to a point and diminishing together, an "association syndrome." In addition, general signs are often more marked with encephalitis than with abscess—headache is severe and continuous, slight changes in the eyegrounds occur early and the temperature is raised.

If these observations are put in more general terms it will be seen that the process and its signs are precisely the same as those which occur when infection attacks any other region of the body. At the onset there is the general disturbance caused by the invasion, together with local signs of the attack. If the process resolves without suppuration, general and local signs subside together, as in encephalitis. If, on the other hand, suppuration takes place, the general signs improve as the pus localizes, though the local signs increase until an exit is given to the pus.

Nevertheless, it must be admitted that the elucidation of the problem can be exceedingly difficult, and in some cases it will not be possible except by an exploratory puncture. It is often hard enough to decide whether or not suppuration has occurred even in regions which can be seen and palpated, so that it is scarcely surprising that great difficulty is encountered in interpretation of signs produced by so guarded and complex a structure as the brain.

J. D., a Negro aged 21, was admitted to the neurosurgical service of the Bellevue Hospital on Oct. 7, 1937, with the history that seven days previously he had been struck on the left parietal region with a piece of lead piping. The resulting wound in the scalp had been sewn up without probing or roentgen examination. Four days later he complained of stiffness of the neck and weakness of the right hand. On admission the stiffness of the neck had improved, but he had fairly severe headache; the weakness of the hand had increased, and there was also some weakness of the right leg.

Examination.—A suppurating wound was present in the left parietal region, with a temperature of 102 F. and weakness of the right side of the face and right arm and leg. Tendon and abdominal reflexes were absent on both sides; the left plantar response was flexor, and the right was doubtful, but certainly different from the left; the eyegrounds were normal; the spinal fluid was not under pressure and was clear and contained 4 cells per cubic millimeter. A roentgenogram showed a depressed comminuted fracture of the left parietal bone.

Diagnosis.—A diagnosis of localized encephalitis was made, with the possibility of an abscess in mind, and it was decided to wait on events.

Progress.—During the first week the wound cleaned up with treatment and the temperature became normal, but headache and the neurologic signs remained unchanged. The spinal fluid pressure was 220 mm. of water; no cells were present, and a culture was sterile.

During the second week all signs increased. Headache became more severe, with nausea; there was marked weakness of the whole right side; all tendon reflexes were still difficult or impossible to obtain, but the right plantar response was now definitely extensor and there was astereognosis in the right hand. The spinal fluid pressure had risen to 300 mm. of water; there were still no cells. It was decided to explore the wound.

Operation (Oct. 22, 1937).—The wound in the scalp was explored, and a number of depressed fragments of bone enclosed in dense scar tissue were removed. There was no pus; the dura was intact and pulsated feebly; the brain, therefore, was not explored. The wound was partially closed.

On each of the following two days the patient had a convulsion involving the whole right side, but the neurologic signs remained unchanged. At the end of a week (October 29) the wound was almost healed; the headache was greatly improved and the right limbs were stronger; astereognosis was still present.

Encephalogram.—A month later signs persisted on the right side, although the headache had disappeared. An encephalogram therefore was made and showed slight dilatation of the left ventricle and distortion of the upper border, suggesting the pull of a scar. The spinal fluid contained 2 cells per cubic millimeter.

After the examination, the patient improved rapidly and ten weeks after the injury (December 13) was discharged from the hospital, free from neurologic signs except for astereognosis in the right hand.

This case is a good example of the group, except that at no time was there any increase in cells in the spinal fluid, a fact to be explained presumably by the low virulence of the infection.

II. *Acute Hemorrhagic Encephalitis.*—The hemorrhagic type of infective encephalitis gives a more characteristic picture than the simple form, a picture quite unlike that of an abscess although often diagnosed as such. The onset is acute, usually occurring in the course of an original acute infection; the evolution is rapid, as is the devolution if the patient recovers; the mortality is high—4 of the 8 patients in my series died.

The feature in this group is the association with early widespread focal signs of marked mental excitement, incoherence, even noisy delirium and a restlessness which may require restraint—an encephalitic picture so different from the drowsiness or stupor characteristic of an abscess that it is surprising that the two should so often be confused. Occasionally there are convulsions, either as the first sign of cerebral invasion or in the course of the disease. Daily variations occur in the condition of the patient which are much more marked than the variations in cases of abscess, but which arise presumably from the same cause—changes in the amount of surrounding edema. A low degree of papilledema is common. The temperature is high; the pulse rate is raised in proportion. The spinal fluid is under pressure, with an

increase in cells, again to be counted in hundreds, but in this case the increase is mainly in lymphocytes. And here, again, there is the association syndrome—focal signs and findings in the fluid rising and falling synchronously.

K. D., a woman aged 57, was seen on Oct. 14, 1933, and gave the history that for four weeks she had had a discharge from the left ear, which had started in the course of an attack of influenza. In the previous few days there had been pain around the ear with fever. Examination showed an evidently widespread infection of the mastoid, with no signs of any complication. Operation the next day revealed a large abscess in the tip of the mastoid, with the lateral sinus exposed and covered with granulations but not thrombosed; the dura of the middle fossa, when exposed, appeared normal.

Five days later, the patient had a chill and became wandering and restless, but without other neurologic signs. The spinal fluid contained 4 cells per cubic millimeter, all of which were lymphocytes. Two days later (October 22), on account of continued swing in temperature, the lateral sinus was occluded and the jugular vein tied. The patient had two more chills only.

On October 27 she was wandering and had slight signs on the right side. On October 29 she was very ill; the temperature was 101 F.; she was confused, wandering and extremely restless; there were complete right hemiparesis and aphasia and slight swelling of both optic disks; the spinal fluid was under a pressure of 300 mm. of water, with 160 cells, 86 per cent of which were lymphocytes. Decompression was done; the dura was tense, and there was an area of thickening above the tegmen. A small incision was made, which released only a little faintly turbid fluid. The brain was not explored.

The patient was treated subsequently by means of intravenous injections of dextrose and spinal punctures; she made steady improvement. When she was discharged on November 28 all neurologic signs had disappeared; the aphasia had completely recovered, and in August 1935 the patient reported that she had completely regained her former health, although it took a year to do so.

III. *Serous Encephalitis.*—As in the preceding group, a definite clinical picture emerges, and one which often goes unrecognized. A patient with an active infection in the skull is suddenly and without warning seized with a convulsion. This convulsion, often of jacksonian type, may be followed by others, each of which leaves increasing residual paresis, until there is eventually complete contralateral paralysis. The lesion may extend deeply enough to produce profound aphasia in cases of lesions on the left side, and in 1 case I have seen complete hemiplegia and hemianesthesia, which cleared in a few hours. These rapid involvements of large areas can be caused by nothing else than by edema, and there need not be any underlying suppuration in the brain itself to cause the edema. The temperature may be slightly raised; the spinal fluid is often under moderately increased pressure and shows a small increase in cells, mainly polymorphonuclears. If drainage of the primary focus is undertaken promptly, the neurologic signs clear completely in twenty-four hours or so, and there are no further convulsions, a dramatic transformation.

The importance of recognizing this picture for what it is, an attack on the dura which has produced cerebral edema, is that delay shall not take place in dealing with the dural condition. In all cases in which a convulsion is the first sign of intracranial extension from an obvious focus, the focus should be drained immediately or reexplored in search for some dural involvement overlooked at or arisen since the first operation. That found, exploration of the brain should be deferred, and will probably never be necessary. Promptitude is the essence of the contract, lest serous encephalitis turn into infective.

C. D., a girl aged 7 years, was admitted to the Manhattan Eye, Ear and Throat Hospital, service of Dr. John R. Page, on Feb. 7, 1937, with acute mastoiditis on the right side. The mastoid was drained on the day of admission, and pus was found under pressure, together with a pathologic exposure of the dura which was covered with granulations. No extradural abscess was present. The wound was packed, and the postoperative course for the next two days was uneventful. On February 9, at 10 a. m., after a dressing during which the packing had been changed, a generalized convulsion took place, which lasted for ten minutes, and the child became unconscious. At 1 p. m., another generalized convulsion, of five minutes' duration, occurred, and this time the packing was removed.

Examination.—At 2:30 p. m. (i. e., four and a half and one and a half hours, respectively, after the two convulsions) the child was seen by me. At this time she was semiconscious and had complete left hemiplegia and hemianesthesia. There was no papilledema; a spinal tap was not done. The mastoid wound appeared satisfactory and the dural exposure clean.

Twenty-four hours later the child had completely recovered, no vestige of hemiplegia or hemianesthesia remaining except for slight increase of tendon reflexes on the left side.

The child had no more fits and was discharged from the hospital on March 3, with the wound healed and no neurologic signs other than a doubtful left plantar response.

Subsequent Progress.—Except for some trouble with healing of the mastoid wound, which required a second operation, the course was uneventful; there was no recurrence of any neurologic condition, and three months later the child was reported to be well.

This case demonstrates admirably the sudden onset of the edema in these cases and how widespread it may be, in this instance extending deeply enough to involve the thalamus. It demonstrates, also, how rapidly and completely the edema disappears once the cause—in this instance, no doubt, too tight a packing, but often an extradural abscess—has been removed.

TREATMENT

Little remains to be said about treatment. The essence of it is to make sure of complete drainage of the primary focus and removal of any source of dural involvement, but to avoid exploration of the brain unless by this means only can a diagnosis be made. Exploration here,

as elsewhere, may convert a nonsuppurative into a suppurative lesion or provoke activity which may result in perforation of the ventricle. In cases of the simple type it matters less and, indeed, may be the only way of settling the diagnosis, but in cases of the acute hemorrhagic type exploration should not be necessary to diagnosis and is actively dangerous. Four of 8 patients in my series with the acute condition died, and 3 of the 4 had had an exploratory operation, while of 5 who were not subjected to exploration only 1 died. Decompression, both from without, by removal of bone and from within, by dehydration, is helpful, especially in cases of the acute type, but the dura should not be opened.

SUMMARY

1. A plea is put forward for the recognition of localized nonsuppurative encephalitis as a clinical entity.

2. The condition is integrated pathologically with localized infection of the brain as a whole, and three varieties are described.

3. An attempt is made to present a clinical picture of each type whereby it may be differentiated from the others and from an abscess.

4. The inadvisability of exploration of the brain and therefore the importance of accurate diagnosis are emphasized.

Case Reports

TUBEROUS SCLEROSIS

Relief of Epileptic Symptoms by Radiation Therapy

ASA B. FRIEDMAN, M.D., BROOKLYN
Radiation Therapist, Kings County Hospital

The rarity of tuberous sclerosis justifies the adding of an additional case to the small group already recorded in the literature. Only 1 patient with this disease has been encountered among more than 6,000 admitted to the radiation therapy service of the Kings County Hospital.

Tuberous sclerosis is characterized by diffuse multiple nodular tumor-like accumulations of primitive glial tissue in the motor cortex of the brain. Associated with these there are other ectodermal developmental abnormalities, such as adenoma sebaceum facialis, rhabdomyoma of the cardiac muscle, embryonic muscle-like tumors in the kidney and phacomas in the retina. The histologic picture of the cortical lesions is largely an accumulation of spongioblast-like primitive glial cells. In the depth of these nodules or nests of cells may be deposits of hyaline material or calcium salts, besides many giant cells and evidence of fatty degeneration.

The classic clinical picture is the triad of progressive retardation of mental development, epileptic seizures and adenoma sebaceum facialis. The clinical history frequently shows a familial or hereditary strain. In many of the reported cases incomplete variants of the disease have involved 1 parent or brothers or sisters. Two cases were reported in which identical twins were involved. In many cases there was idiocy or epilepsy of varying degree in a parent, although the diagnosis of tuberous sclerosis had not been made. Occasionally, as in the case here reported, there is no familial history. While the triad of symptoms just described is characteristic, variants may exist in which the mental development remains normal or in which the predominant symptoms are those of cerebral tumor.

The usual treatment of this condition consists of the use of adequate doses of the barbiturates and the institutional housing of the patient, but in the case herein reported treatment consisted of roentgen therapy to the entire brain.

Spontaneous remissions in symptoms have been reported, and in 1 of Macdonald Critchley's cases a seven year spontaneous remission in epileptic seizures occurred. Unfortunately, that patient showed continued progressive mental deterioration. The improvement obtained in my case followed so soon after radiation therapy, and the results after this treatment were so definite, that it is reasonable to attribute the

From the Division of Cancer, Department of Hospitals, New York, Dr. Ira I. Kaplan, Director.

relief of symptoms directly to the treatment given. Furthermore, a subsequent recurrence of motor symptoms was relieved by additional irradiation.

REPORT OF A CASE

A. Z., a white girl aged 17½, came for treatment on Jan. 5, 1935. The past history was essentially without significance, and the family history gave no evidence of this condition. For about six months prior to her first visit to this service she had been receiving ultraviolet radiation from a dermatologist, because of a red elevated eruption on the forehead, nose and cheeks. In May 1934, while in school, she had her first attack of epilepsy. There was a tightening of the facial muscles, followed by frothing at the mouth and syncope. She recovered from this attack and felt well for several months, except for periodically recurring paresthesia, a sense of numbness in the right arm and frequent twitchings of the right side of the face. In December 1934 she had a second epileptic seizure. In July and August 1935 there were numerous milder or more severe epileptic seizures, sometimes occurring three or four times a day.

Physical Examination.—When first seen the patient was well developed, mentally alert and intelligent. A number of lesions of adenoma sebaceum covered both cheeks and the nose. There was slight facial weakness on the right side. The fundus of one eye presented an elongated bulblike phacoma on the nasal side. There were no other neurologic signs. Intelligence was normal, and the patient was maintaining her level in high school without difficulty. Her behavior and emotional reactions were normal. Roentgen examination of the chest showed no abnormality. The cardiac rate and rhythm were normal. The blood pressure was 120 systolic and 80 diastolic. The abdomen and extremities were essentially normal. A blood count showed no evidence of anemia and no abnormal cells. Kahn and Wassermann tests were negative.

The presence of adenoma sebaceum, a history of epileptic seizures and the finding of a characteristic nodule in the retina justified the diagnosis of tuberous sclerosis, even in the absence of mental deterioration.

Treatment.—Roentgen therapy was started on Jan. 7, 1935, and continued until April 2, 1935; a total dose of 850 r was applied during this time to each of four fields, covering together the whole skull. The factors used were 180 kilovolts, 0.5 mm. of copper and 1 mm. of aluminum filtration and a focal skin distance of 40 cm. Before the end of the treatment the motor symptoms had markedly diminished, both in severity and in frequency. Some epilation occurred as a result of treatment.

On May 28, 1935, treatment was resumed because of a recurrence of symptoms. An additional 850 r in divided doses was given to each lateral field of the skull between May 28 and Sept. 9, 1935.

Since completion of treatment in September 1935, the patient has remained free from symptoms. Epilation was fairly complete, but the hair later regrew; the patient wore a wig during the interim. Mentally she has remained normal and is at present employed as a clerk in a large industrial organization. Adenoma sebaceum is still present.

CONCLUSIONS

A case of tuberous sclerosis without mental deterioration treated with roentgen therapy is reported. Relief of epileptic symptoms was obtained. The patient has remained well for over two and one-half years.

257 New York Avenue.

BIBLIOGRAPHY

Berkwitz, N. J., and Rigler, L. G.: Tuberous Sclerosis Diagnosed with Cerebral Pneumography, Arch. Neurol. & Psychiat. **34**:833-838 (Oct.) 1935.

Critchley, M., and Earl, C. J. C.: Brain **55**:311-346, 1932.

Fabing, H.: Brain **57**:227-238, 1934.

Gottlieb, J. S., and Lavine, G. R.: Tuberous Sclerosis with Unusual Lesions of the Bones, Arch. Neurol. & Psychiat. **33**:379-388 (Feb.) 1935.

Grinker, R.: Neurology, ed. 2, Springfield, Ill., Charles C. Thomas, Publisher, 1937.

Jelliffe, S. E., and White, W. A.: Diseases of the Nervous System: A Text-Book of Neurology and Psychiatry, ed. 5, Philadelphia, Lea & Febiger, 1929.

van der Hoeve, J.: Tr. Ophth. Soc. U. Kingdom **52**:380-401, 1932.

Wechsler, I. S.: A Text Book of Clinical Neurology, ed. 2, Philadelphia, W. B. Saunders Company, 1931.

ANALYSIS OF THE THINKING DISORDER IN A CASE OF SCHIZOPHRENIA

EUGENIA HANFMANN, PH.D., CHICAGO

In attempting to characterize successive stages in the development of thinking, one has often made the distinction between concrete, situational thinking and abstract, conceptual or categorial thinking. In the first the person's thinking and acting are directly determined by the immediate situation in its concreteness and singularity; in the second the person tries to master the situation by applying to it certain categories or concepts. These two ways of perceiving the world, which have repeatedly been described as the two major stages in the development both of the individual person and of society or culture, have been used also for characterization of certain pathologic conditions. Gelb and Goldstein have convincingly demonstrated that in patients with cerebral lesions there is a striking loss of the conceptual approach to the world, or of the "categorial attitude," as they termed it. They showed how this loss accounts both for changes in the patient's general behavior and for defects in specific performance.

The results of recent investigations suggest that disturbances of thinking observed in schizophrenic persons may also be explained in terms of a greater primitiveness and concreteness of thinking. Similarities between the thinking of schizophrenic patients and that of primitive peoples have been repeatedly pointed out,[1] as well as analogies between the thinking of schizophrenic persons and that of patients with defects of organic origin.[2] Vigotsky,[3] the Russian psychologist, was the first investigator who on the basis of systematic experimental investigation of the thinking processes of different groups of patients reached the conclusion that schizophrenic patients show a reduction of conceptual thinking comparable in kind with that observed in patients with cerebral lesions. These results were confirmed by other investigators. In applying the concept formation test introduced by Vigotsky, Kasanin and I[4]

From the Department of Psychiatry, the Michael Reese Hospital.

This investigation was financed through the National Committee for Mental Hygiene from funds granted by the Committee on Research in Dementia Praecox, founded by the Supreme Council, 33 Degree Scottish Rite, Northern Masonic Jurisdiction, U. S. A.

1. Storch, A.: The Primitive Archaic Forms of Inner Experience and Thought in Schizophrenia, Nervous and Mental Disease Monograph 36, New York, Nervous and Mental Disease Publishing Company, 1924.

2. Bychowski, G.: Certain Problems of Schizophrenia in the Light of Cerebral Pathology, J. Nerv. & Ment. Dis. **81**:280, 1935.

3. Vigotsky, L. S.: Thought in Schizophrenia, Arch. Neurol. & Psychiat. **31**:1063 (May) 1934.

4. Kasanin, J., and Hanfmann, E.: An Experimental Study of Concept Formation in Schizophrenia, Am. J. Psychiat. **95**:35, 1938.

found definite impairment of conceptual thinking in a large number of schizophrenic patients. Bolles and Goldstein [5] and Cameron,[6] working with different methods, arrived at similar conclusions.

The question which arises next is that of the exact nature of this defect and its role in the total schizophrenic picture. This question can be answered only through a detailed analysis of single, clearcut cases, an analysis based on both experiments and clinical observation. In the present study I attempt to give such an analysis of a representative case of schizophrenia in which the disturbance of thinking was a prominent trait.

REPORT OF A CASE

Clinical History.—J. C., an American woman aged 23, after graduating from grammar school, where she was considered a good student, became a mill worker. At the age of 21 the first psychotic symptoms appeared, and a year later she was committed to a state hospital. This investigation was made two years after the onset of the psychosis. The patient at that time presented a typical schizophrenic picture, was withdrawn and preoccupied when left alone, had auditory hallucinations and in response to them became at times excited and destructive. Usually, however, she followed the hospital routine willingly and rather automatically. The psychiatric summary described her as well oriented, having clear consciousness and well preserved memory. In her preoccupation she was concerned with her sexual role and with her relations to the man whose voice she heard in her hallucinations. She showed strongly ambivalent feelings toward both parents, especially toward the father, and at times seemed to doubt that he was her father. There were also feelings of guilt because of sexual impulses and strong feelings of inferiority. All this emotional content, however, was seldom revealed and colored only slightly the patient's behavior in the experimental situation.

She was eager to "study," as she called it, and often came to the examiner's room of her own accord, asking to be given something to do, so that it was easy to present the tests to her. She was chosen for an intensive study because of this willingness and superficial accessibility and also because she had displayed an extremely poor performance in the concept formation test.[4]

Special Tests.—A number of tests designed to reveal the different aspects of the thinking disturbance were given. I shall first discuss the results of some of these tests and on this basis attempt a general characterization of the disturbance. I shall then try to explain the effects of this disorder, as revealed by the test, on the particular clinical picture presented by the patient.

Interesting observations were made during the simple tests of reading and writing ability and of memory for sentences. Reading and writing in themselves presented no difficulty. More than that, they were accurate and consistent with the patient's good grades at school. What was conspicuous, however, was the attitude of the patient toward the content of the verbal material presented to her. When a sentence was read to her she almost invariably made comments about its truth or falsity. In the sentence repetition task, for instance, the patient, after repeating a sentence, such as: "When the train passes you will hear the whistle

5. Bolles, M., and Goldstein, K.: A Study of the Impairment of "Abstract Behavior" in Schizophrenic Patients, Psychiatric Quart. **12**:42, 1938.

6. Cameron, N.: Reasoning, Regression and Communication in Schizophrenics, Psychological Monograph 221, Columbus, Ohio, Psychological Review Company, 1938, vol. 50, no. 1.

blow," would add, as if offering a proof for that statement: "Yes, I do hear the whistle blow at night; do you?" When the examiner introduced a "false" sentence: "In summer it snows," the patient repeated it but immediately protested, saying: "No, it does not, because it is June—the flowers are out." Similarly, when during the dictation test she was asked to write the sentence "It is raining," she started to do so but stopped, looked out of the window, remarked that the weather was fine and, instead of the sentence dictated, wrote: "The sun is shining." One is reminded of the behavior of certain aphasic persons who actually cannot repeat or write an incorrect statement. The same tendency appeared in the reading test. While listening to a story read to her the patient often made remarks such as: "Yes, I know it; I see that sometimes," as if attributing a certain degree of reality to the story. When she was asked questions about the content of the story she had just read, she frequently answered them without any reference to the test but in accordance with her own experience or opinion on the subject. Thus, she read a story about a circus parade which mentioned the difference in preferences of boys and girls for animals. In answer to the question about the girls' preferences, the patient pointed to the picture of one of the animals, but continued: "The girls like to go out, to play, to study. I will put the girls like to walk, to call up, like to be dressmakers." In spite of all explanations that the questions referred to the text, she persisted in this method of answering them independently of the story and in accordance with reality as she saw it. If the story, however simple, dealt with topics outside the sphere of her personal interest or experience, as was the case, e. g., with fables dealing with wild animals, the patient could only with difficulty be made to listen to it or to repeat it. Sometimes, yielding to the examiner's coaxing, she remarked with an air of indifference: "This is just so we get some work done!" The story that could not be related to the patient's conception of reality was merely an object of artificial activity, such as reading, and had no meaning apart from that. One is again reminded of patients with injuries to the brain who are not able even to listen to a story. Such a patient, on hearing the first words, looks around the room for the persons or objects mentioned and, not finding them, is unable to comprehend the story. Although my patient showed much more normal behavior in listening to a story, tendencies in the same direction clearly manifested themselves.

Phenomena analogous to those described in the preceding paragraph were observed also when the patient was asked to describe and interpret pictures. She often spoke of them as if they had a reality value. As with the stories, questions referring to the pictures were often answered on the basis of the actual, and not the pictured, situation. Once the examiner showed her a picture representing a boy fishing next to a "no fishing" sign and asked: "Why should he not fish here?" The patient answered, with gestures indicating that she spoke of her actual surroundings: "They don't fish here in the hospital—and it is not the time to fish now."

These examples show that the patient was unable to make an unreal assumption or to accept a fictitious situation as such, whether it was expressed in a sentence, a story or a picture. Each sentence for her was essentially a communication. It must have a reality value if it was to have any meaning at all. To assume something just for the sake of argument or for any other indirect purpose was totally against the nature of the patient's ideational life. This was clearly and repeatedly demonstrated. In the "ball and field" test of the Stanford-Binet scale the subject is asked to show by drawing how he would hunt for a ball lost in a circular field. The patient merely declared that she had not lost a ball and refused to show how

she would look for it, saying: "You'll never find it if you did not lose it, and I never lost any." In the course of a definition test she was asked to define the word "judge." She showed displeasure and rejected the task, saying: "I know it, but that has nothing to do with me; it is a man's job." In the task of finding absurdities in the sentences read the patient also showed peculiar behavior. Although told in advance that the sentence would contain "something foolish" which she was to find, she did not merely point out the absurdities when she noticed them. Instead, she either repudiated the incorrect statement or tried to account in some way for the incongruity. Thus, on being read the sentence about "a road from my house to the city which is downhill all the way to the city and downhill all the way home," she tried to explain it, saying: "Sometimes a road looks like a hill and it is straight." This behavior showed that she took each statement at its face value, as a communication and not as an artefact merely to be tested for its logical qualities. She refused or was unable to assume beforehand an attitude of doubt and criticism and to search a sentence for absurdities. For the same reason, she was often unable to realize that the examiner asked her certain questions not to obtain information but merely to test her knowledge; because of its artificiality, she could not fully grasp the examination situation.

Since the patient needed the support of reality even to understand the simple, immediate meaning of a sentence, one would expect that sentences or stories which, besides their primary obvious meaning, have a second and more general significance would be quite inaccessible to her. In fact, all attempts to make the patient understand the moral of a fable or the general meaning of a proverb ended in failure; she understood only the immediate meaning and never saw it as an instance or an illustration of a general rule. On one occasion the examiner attempted to explain that a proverb is applicable to different situations, pointing out that one may say "Don't cry over spilt milk" to some one who is worrying over lost money. The patient was then asked what the proverb would mean in this case. The answer was: "Don't cry over spilt milk because you can go out to the store and get some more milk." Examiner: "But we were speaking about money." Patient: "Yes, maybe you have lost it around the building." The two situations remained isolated for the patient, since she never rose to the level of a general rule which could connect them. She was unable to master the duality of the concrete and the more general meaning implied in proverbs and fables. Language for her, although formally unimpaired, was situational language and that only. It could be used for communications based on reality, but it did not become, as it does with normal persons, an efficient tool for abstract thinking.

Leaving the field of language, I turn to tasks of a different nature; namely, those in which the patient is given a number of objects and has to organize them in some way. As has been shown in many investigations, the response to this type of task shows clearly certain characteristics of the subject's thinking.[7]

In the first experiment of this kind the patient was given a number of small pictures of different objects, schematically but clearly drawn. The pictures were spread on the table in a haphazard arrangement, and the patient was asked to sort them, putting together the objects that she thought belonged together. A normal person when given this task would quickly organize all pictures into large groups, such as persons, animals, plants, tools, household utensils, vehicles and the like. The patient when asked to place together objects of the same kind at first declared that there was only one picture of each kind. She would not

7. Weigl, E.: Zur Psychologie sogenannter Abstraktionprozesse: I. Untersuchungen über das "Ordnen," Ztschr. f. Psychol. **103**:1, 1927.

group them in any way, but named or described each picture separately. When the examiner pointed out that certain pictures might be grouped together, e. g., because they all represented animals, the patient disagreed and emphasized the individuality of each, saying, for instance: "Yes, but they go to different places; the cow goes in the barn, the hare in the fields." It took a great deal of urging and help on the part of the examiner to make the patient attempt any grouping at all. When she did attempt it she did not try to organize all the pictures into larger groups as would a normal person; the associations she made seldom extended to more than two or three objects. The following are a few examples of such associations. The picture of a nest and that of a tree were placed together with the explanation "you find the nest on the tree;" a dish was placed with a cup because "we can put the cup in the dish"; a coat, with a baby because "baby wears a coat"; a child, with a cup "because the child drinks out of a cup." A fish was placed with vegetables because "fish goes with the pumpkin"; when the examiner transferred it to the group of animals the patient at first objected and then, noticing the picture of a cat, said, as if with sudden insight: "Oh yes, the cat eats fish; sure." It is readily seen that the objects were grouped not on the basis of belonging to the same general class (such as animals or plants) but for one of two reasons: Either they occurred together in space or they were parts of the same action. In both cases the objects were seen as belonging to a concrete spatial-temporal complex and not as members of an abstract class. Sometimes objects were placed together which to the normal person seem to represent a definite class, such as animals, tools or furniture, but when the patient's explanations are taken into account one sees that to her these groups were essentially spatially determined complexes. The animals were declared to belong together because they are found outside, "because sometimes when you walk you see them." The group of tools was designated as the cellar and that of furniture as the girl's house, and later other objects were added to this group with the explanation: "You could also find a coat in a girl's house, and a man." When the examiner placed together three pictures representing persons, the patient agreed: "Yes, the girl could stay with the man and the baby." Later she put the picture of the baby farther away, saying that the baby liked to play alone. The difference between this concrete bond of "living together" and the common "belongingness" in a general category, such as that of "human beings," is obvious. Summarizing the results of this experiment, one may say that the patient considered single objects as individuals and never as representatives of a class. If she had to group these objects she did so on the basis of concrete situations or of casual associations between the individual objects and not on the basis of abstract similarities.

Among the tasks given the patient was one that had a structure analogous to the task of sorting, i. e., the task of finding similarities between two or more objects named by the examiner. The results of this test supplement and confirm those of the sorting tests. If the objects named suggested an obvious similarity and evoked the same concrete situation the patient occasionally solved the task adequately. Thus, she was able to tell that wood and coal both burn, that apple and peach are both eaten. When more than two objects were named and the point of similarity was less concrete, there were failures of the same kind as in the sorting of pictures. Although in this test the instructions require explicitly the naming of similarities between objects, the patient might form concrete complexes of an entirely different nature. Thus, when asked for a similarity of a book, a teacher and a newspaper, she answered: "The teacher reads a newspaper and a book." At another time she declared that they were all alike because "a book is for reading; a teacher uses the book, and a newspaper is like a book, isn't

it?" Two objects were connected by action and two by similarity, and the patient thought that they all belonged together. In other instances she simply denied all similarity of the objects named, describing each separately or insisting that they were all different. This sometimes happened even with objects for which the similarity had previously been correctly given. Success or failure depended simply on the traits of the objects which happened to strike the patient at a given time. Wood and coal were found similar by the patient at one time, because they both burn; at a later date, however, she insisted that they were totally different, since one is brown and the other black. There was no active search for similarities on the part of the patient, as there was no active attempt in the sorting experiments to organize the totality of the pictures. If the objects named did not evoke by themselves an idea of similarity the patient could not do anything about it. If of three objects named only two formed a natural unit she merely omitted mention of the third object. She was unable to survey the objects actively with the purpose of finding a group into which all would fit and did not realize that the point of view may be changed arbitrarily. Once a similarity had presented itself to her, it was the similarity; she did not conceive the possibility of another.

To illustrate the difficulty of finding a similarity among three objects named, I may cite the record of another schizophrenic patient, who in this respect presented a clear picture. On hearing the names of the three objects he usually repeated them in an astonished tone, as if startled by their being mentioned together, and then named a similarity between the two objects of the three which easily formed a similarity unit. For example, "book, teacher, newspaper" evoked: "Book and newspaper are both reading matter"; "Wool, cotton, leather"; "Wool and leather are both durable." Examiner: "And cotton too?" "Not in respect to wool and leather!" To "rose, potato, tree" the response was: "Rose and tree are both foliage . . . Oh, did you say potato plant or just potato?" "Potato." "Then just two of them." Here the patient attempted to fit the third object into the complex evoked by the first two objects, but failed because of his rigid dependence on words. For him each object had a name and only one name, and he rejected the idea that the same generic name might be given different objects or the same object be described by different names. Since the word "potato" could not be taken as signifying a plant, it was simply left outside the evoked complex "foliage." No attempt was made to find a category that would include all three objects.

Thus, the questions on similarity, besides confirming the results of the sorting experiments, bring out especially clearly the passive attitude of the patient as compared with the conceptual approach, which is characterized by an active search for similarities.

Sorting of pictures was supplemented also by sorting of colors. In this test she committed none of the gross errors occasionally made by a patient with a cerebral lesion.[8] Thus, in sorting the Holmgren wools she did not place together skeins totally different in hue; with a skein as a sample she could pick out all the nuances of the same color. Yet she did it unwillingly, all the while remonstrating that in reality they were different and should not be put together. "This is a different green —see what I mean? The regular way you could put only one together [i. e., each nuance by itself]. If you were working in a mill you would put one together, so they don't get mixed when you make a ball with them, see?" To place together the different nuances was an incongruity for the patient because for her they were individual colors, not representatives of one general hue. Even in sorting blocks

8. Gelb, A., and Goldstein, K.: Ueber Farbennamenamnesie, Psychol. Forsch. **6**:127, 1924.

painted in only four colors the patient met with difficulties. The smallest differences in brightness caused by the fact that some of the blocks were dirtier than others and also differences that had nothing to do with color as such made her hesitate in putting blocks together: "This is entirely different, because it has got little holes in it. This looks like a dirty yellow. These are different blues. And this one is a different shape."

The inability to abstract from any aspect of the offered material was also responsible for the patient's failure in the Kohs cube test. In this test the subject is presented with colored patterns painted on cards and is told to build up the same designs out of wooden cubes the sides of which are painted in different colors. This test has been analyzed by Goldstein, who used it both with schizophrenic patients and with patients with cerebral lesions.[5] Since the performance of my patient corresponded exactly to the picture described by Goldstein, I shall not describe it in detail. Generally speaking, failure occurred because the patient was unable to abstract from the differences of size, dimension and outline which exist between the design drawn on the card and that reproduced with the blocks. It was impossible for her to disregard any aspect of the material and to consider only the aspects which were essential for the task at hand. Even when the examiner made the model out of blocks and asked her to reproduce it she was worried by the fact that the sides and under surfaces of the blocks differed in color in the two constructions, although this had nothing to do with the design on top.

All the tasks thus far described reveal the characteristic pattern of the patient. She was dependent on the given material as it impressed her at a given moment and was unable to organize it spontaneously by applying to it certain categories or points of view. There is, however, another point to be considered. In all the tasks in which the patient failed or achieved only poor results, she often showed extreme restlessness while working or even tried to drop the tasks. Although she never directly refused to perform any test and kept telling the examiner: "I get you; I know what you mean," actually she often substituted another activity for the one required of her, e. g., describing pictures or colors for sorting. One might ask, therefore, whether her failures were not due to a general lack of attention and perseverance.

In this case one would expect to find occasional weakness or fluctuation of attention in all the tasks, regardless of their nature. This, however, was not the case. In a number of tasks which will be described later the patient invariably showed great perseverance and good attention. Also, she seemed to gain great satisfaction from these activities. When engaged in them she gave an impression of content and calm, strongly contrasting with her nervousness during the occupations already described. Following Goldstein's terminology, one may speak of the occupations in which the patient functions harmoniously as "adequate tasks." The following questions must then be asked: Do all the adequate tasks have certain characteristics in common which make them acceptable and gratifying to the patient? If so, what are these characteristics? In order to answer these questions one must at first consider the tasks separately.

The patient's favorite task was the one which she called "dictionary work." It consisted in copying from the dictionary all the words on a page with their explanations. Several pages were copied in this way without mistakes, but no attention was paid to the meaning of the words, and not a single new word was learned by the patient in the course of this "dictionary work." Similarly, whole pages were copied from other books without the patient having any idea of the content of her writing. The utterly mechanical nature of her copying was clearly revealed

when the examiner asked her to copy only certain names from a catalogue in order to make a mailing list. The patient was unable to follow even the simplest rules of selection, such as copying only the names marked or omitting the degrees following the names. Only the most striking marking of everything that had to be copied led to partial success. The copying of drawings was also often undertaken by the patient; it was done as thoroughly as the copying of print. Thus, the series of drawings representing the same design with slight variations only (Stanford-Binet scoring card for designs) was rendered correctly to the smallest detail.

Another favorite occupation of the patient might be designated as "taking an inventory" of her surroundings, an activity which reflected her unusual interest in the objects around her. Even while occupied with some task, she often stopped to examine an object at which she happened to glance or to make a remark about it. At other times she made more systematic investigations, walking around in the room, picking up or touching one object after another and all the while commenting and inquiring about them. "A basket—what is this nice to put in? This is nice paper—can I touch it? It is yellow. This piece is pink. What is this—a pencil sharpener? What do you do when you want to clean it? That is a telephone book, isn't it? Who made these pictures? Did you snap them? You don't know who snapped them?" This eager desire of the patient to investigate the objects in the room and to determine their function reminds one of the behavior of patients with agnostic symptoms, who sometimes start spontaneously to investigate their environment, rejoicing in every recognition of an object. Often the patient was not satisfied with naming or describing the objects but took a sheet of paper and wrote down their names or made drawings of them, displaying the same attention to detail as in her copying activities. She was best satisfied if she could place an object on paper and trace its outline. Sometimes she wrote on the drawing, thus combining the two methods of "inventory taking." She made, for instance, a detailed picture of the plant in the examining room and wrote "straw" on the part showing the flower stand to designate the material of which it was made; under the drawing she wrote: "In the plant we put water to keep it green." In spite of her mastery of the technic of drawing, the patient never drew anything without a model. In her literary productions the situation was the same. When urged by the examiner to write a story she had recourse to description of the momentary situation and delivered "stories" of the following type: "We are working at twenty past 1 [she had asked the examiner about the time]. We read books to study. The room looks very neatly. I come in every day to study with Dr. H. The radiators are heated. Keep windows open for air. The desk has many books to read. There are many buildings here that are made of brick and stone." The patient herself fittingly described her literary activities as "making sentences about things."

In reviewing and comparing the tasks just described, one finds that they are all characterized by exact reproduction of some given model. This finding provides an answer to the question as to what it is that makes a task adequate for the patient. She succeeded and obtained satisfaction from her work when she was not required to organize the material spontaneously but could center and anchor her activity in a single object. She was best satisfied when she could copy her material step by step. The unswerving attention displayed by the patient in this occupation was not the cause and explanation of her success but was itself only a consequence of the particular structure of the task. The patient completely accepted the tasks that she could solve, trying to escape or to modify those for which she had no adequate means of solution.

The analysis of the adequate tasks thus confirms indirectly the results obtained from the analysis of tasks in which the patient failed. Both her failures and her successes in different fields point to one underlying factor. All her performances were determined by the material, by the actual situation and by concrete reality, and this dependence was practically absolute. Within the sphere of concrete material she could make the finest discriminations between qualities, observe and point out the smallest details of objects and render them correctly through any means of description available to her. Yet she was unable to make any voluntary selection from these data or to organize them according to any principle—she was actually at the mercy of the given material as it impressed her at a given moment, and she could not detach herself from the given situation. She was unable to see a thing as representing something else: to see a skein of wool as a sample of a color, a picture of a horse as representing a class of animals or a story or saying as representing or exemplifying some general rule of behavior. To maintain the duality of the immediately given and that which it represents was outside her possibilities.

The patient thus presented in the extreme the loss of the categorial attitude and a reduction to the level of concrete, situational thinking and acting. Definite indications of such primitivization have been found in many schizophrenic patients, but whereas in most cases this defect appears as one trait among others, in this case it seemed to play the central role in the psychotic picture. This patient illustrated a type of intellectual disturbance found in schizophrenia which has been defined by Kasanin as a "primary thought disorder." In cases of this disturbance the thought disorder stands in the center of the clinical picture. It develops rapidly and leads to profound intellectual deterioration.

My patient's failure in all tasks requiring the categorial attitude was striking and extreme, approaching closely the behavior displayed by patients with cerebral lesions. Furthermore, the defect in this case was not obscured by any bizarre productions typical of other cases of schizophrenia. Practically all the failures and shortcomings revealed in the tests could be traced directly to the same general impairment.

If the primitivization of thinking had as important a part in the structure of the patient's psychosis as appears from the tests, one would expect the effect of this disturbance to be apparent also in the patient's behavior outside the experiments. One of the most conspicuous characteristics of this behavior was a peculiar lack of orientation. Viewed superficially, the patient seemed oriented for person, time and place. She knew the name of the hospital and recognized that the persons around her were physicians and nurses. Yet closer examination showed that she had not full insight into the nature of the institution or into the essential factors constituting it. Rather, her conception of the situation was characterized by a peculiar displacement of emphasis from the essential to the less important aspects. This inadequacy became clear when the patient attempted to explain to the examiner the reasons for her dislike of the hospital. This house was too big, she said; she did not like to be in such a big place; she liked to live in a small house or in a small room because, as she put it, "in a small place you can lie down on a couch after dinner, can go out into the yard and hang clothes, can go to town." Here she never went out; she would have liked to go to the city on a bus "in a regular way, as I was taught." In admiring the furnishings of the examining room, she contrasted them with the bareness of the wards: "Outside there is nothing there; I feel better when I study, sit in a cozy little room like this one."

These complaints conveyed vividly to the listener that the patient was depressed by institutional life, with its compulsory routine and lack of freedom. When the examiner once met her usual complaint about the size of the rooms by saying that a movie theater is large, too, the patient promptly replied: "Yes, but you go there just for awhile and then go home—you don't live at a show!" Yet usually she was unable to express this general complaint in any way other than by referring to particular, concrete situations, apparently not relating them to each other. The social structure of the hospital—the relative roles of the physicians, the nurses and the patient—was also not clear to her. For instance, she seemed to feel that the examiner's life was better than her own, a life which the patient took as her ideal, saying: "When I go home that's how I live—like you! I will have a new dress, and I'll fix my hair and keep clean." On the other hand, however, she was unable to conclude from this difference that the observer's status in the hospital was different from her own; she was astonished to find that the observer did not eat with the patients and came and went as she pleased. Hearing that the observer came from another town, she said sympathetically: "Oh, you are lost here, too! . . . You don't like to be here; you want to live in a small room by yourself, don't you!"

The lack of orientation found expression also in her constant complaints about being lost, not knowing her way about and not knowing anything about the actions and purposes of persons around her. In speaking about her fear of getting lost on the hospital grounds, she asked the examiner with astonishment: "You can come from any side and don't get lost?" In speaking of the other patients, she said: "I don't want to get lost with those girls walking around. I do not know who they are and where they are going—maybe they have to go to their homes." On hearing steps in the next room, she asked: "People are going out—are they going out for their own business? Do they work in offices like we do?" On having had to wait in a strange ward, the patient complained: "I don't want you to put me there because there are so many doors there, and I don't know where to go. They should have names on them, like doctor's office, or nurse's office." In trying to overcome this feeling of disorientation she often declared emphatically that she was not afraid of getting lost, that she remembered all places. Once she attempted to draw a map of her surroundings; she made a cross on it and, pointing to this, said: "I have to keep close to my mark so I don't get lost with the girls." The examining and explaining of this map seemed to give her great reassurance.

COMMENT

How can this clinical picture be related to findings in the experimental situation? It is probably in accordance with the prevailing conception of schizophrenia to explain this particular kind of disorientation by the emotional estrangement of the patient from her environment. The results of the experiments described suggest, however, a different explanation. Without denying the importance the emotional factor may have had in the primary production of the disorder, one may assume that the immediate cause of the patient's disorientation is the loss of the categorial attitude. In actual life, as in the experiment, she was unable to transcend the concrete situation and to see it as signifying something else. That is why her complaints were limited to particulars, such as large rooms or strange persons, and gave one the impression of inadequacy. If one assumes that the loss of categorial attitude in this patient was of recent origin and that previously she had

understood normally the wider implications of a situation, it is clear why she had a feeling that something eluded her understanding. This feeling found clear expression in a peculiar question occasionally asked by the patient. While examining objects in the room or working at some task, she would suddenly say, e. g.: "I see it blue—do you see it the way I do?" or "Do you read it the way I do?" and wait anxiously for a reassuring answer. The subjective feeling of disorientation and the recurring complaints about being lost can be traced to this feeling of not being able any longer to understand and to master a situation. The emphatic declarations, on the other hand, of knowing her way about or of understanding the task probably represent her method of fighting this feeling. Her unusual preoccupation with single objects, the taking of the inventory as I called it, can be understood also as representing a fight against disorientation. Feeling unable to grasp the full import of any given situation, she tried to maintain her hold on it by clinging to that which she could grasp clearly, that is, the individual objects with their qualities and functions. They were for her the only terra firma in the uncertain world which eluded her comprehension.

What is the theoretic significance of the analysis of the case here presented? It is not, as may appear, the stressing of the importance of intellectual, as contrasted with emotional, factors in the schizophrenic picture. The reduction or loss of the categorial attitude is to be considered not as a change within the intellectual sphere alone but as a basic disturbance in the functioning of the total organism. The intellectual and the emotional disturbances are probably only two manifestations of the one basic change. Furthermore, the cause of this change cannot be ultimately clarified by means of a psychologic analysis like that just given. The striking resemblance of the patient's behavior to that of a patient with a cerebral injury, while it appears to lend support to the theory of an organic origin of the schizophrenic disturbance, is actually not a proof thereof. The similarity may be merely the consequence of the fact that disintegration of the organism follows the same general lines regardless of the original cause of the disease. The especially strong resemblance of the symptoms in this case to those in a case of cerebral lesion may result from lack of productive elaboration of the primary defect, which in other cases of schizophrenia often tends to obscure the original defect. Whatever the reasons for the particular clarity of the picture presented, the case demonstrates the importance which the loss of categorial attitude may have in certain varieties of schizophrenia. In the case presented this loss not only was one symptom among others but was at the core of the disturbance and enabled one to understand the given clinical picture in most of its specific characteristics.

Attempts like the present analysis to relate various manifestations in a case to the underlying disturbances should replace the mere enumeration of symptoms. Only an analysis that aims at a unitary conception of the symptoms in a case holds the promise of better understanding and more adequate classification of the manifold disturbances which constitute the schizophrenic disorder.

SUMMARY

A case of schizophrenia was subjected to an intensive psychologic study with the view to determine the structure of the thinking disturbance and its role in the total clinical picture. The patient was given a great variety of language and performance tests, particularly tests which required organization of material from some definite point of view, e. g., sorting of pictures or colors. The results of all the tests indicated that the central disturbance was loss of the "categorial attitude," i. e., incapacity to perceive objects as members of a class or as other than concrete and unique. An attempt is made to relate to this central disturbance certain peculiarities of the clinical picture, especially a peculiar disorientation shown by the patient.

BILATERAL FRONTAL LOBECTOMY

Follow-Up Report of a Case

RICHARD M. BRICKNER, M.D., NEW YORK

Bilateral frontal lobectomy in man, with long survival, has been performed only once. The patient, A, has been the subject of previous reports,[1] the last having been made in 1936. The purpose of this paper is to report on A's status to date. He was a stockbroker, born in 1889. Both frontal lobes were removed in 1930.

PHYSICAL STATUS

A's physical status is exactly what it was at the time of the last report. Neurologic examination, when performed on April 1, 1938, gave normal results except that the right achilles jerk was slightly less active than any of the other tendon reflexes and the left cremasteric reflex was absent. It is possible for the first time to report on one of the plantar reflexes, examination of which A did not permit before. In the present examination he allowed the right plantar reflex to be tested; it was normal. A's moderate motor restlessness is present as before, his conversation being interrupted now and then by pacing the floor or performing a "swing" dance, which, he says, is "good—better than you can do it."

The convulsive seizures described in previous reports continued sporadically until May 1937, since when none have occurred. Their form changed gradually—they came to be preceded by an aura in which there were irritability for one day and marked aphasia for approximately an hour. The convulsions became progressively less severe.

PSYCHOLOGIC TESTS

It was intended to repeat all tests which had been performed before, but circumstances made it impossible to carry this out completely. In general, A ranks about as he did before, with a score of 15 years in the Stanford-Binet test, an intelligence quotient of 0.94 and a mental age of 9 years in the Pintner-Paterson scale. Enough tests were performed to show that there has been no great change of a kind which is measurable by the tests, except for the Rorschach observations. In March 1938, A's responses to the cards were closer to the norm than they were in his first examination, January 1936. The Rorschach studies were made by Dr. Bruno Klopfer, who will report on them in detail later. The results of the remaining tests, carried out by Miss Gladys Tallman at the Neurological Institute of New York, are to be reported separately by her.

Read before the Section on Nervous and Mental Diseases, at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 15, 1938.

1. Brickner, R. M.: An Interpretation of Frontal Lobe Function Based upon the Study of a Case of Partial Bilateral Frontal Lobectomy: Localization of Function in the Cerebral Cortex, A. Research Nerv. & Ment. Dis., Proc. **13**:259, 1932; The Role of the Frontal Lobes in Intellectual Function: A Study Based upon a Case of Partial Bilateral Frontal Lobectomy, Psychiat. en neurol. bl. **[38]**: 596, 1934; The Intellectual Functions of the Frontal Lobes: A Study Based upon Observation of a Man After Partial Bilateral Lobectomy, New York, The Macmillan Company, 1936.

BEHAVIORAL STATUS

At the time of observation in 1938 A's symptoms as a group appeared similar to those originally described. They are still to be seen as almost all strung on one thread—lack of complete synthesis of intellectual engrammic products. The same impairment of restraint is present. He still gladly expounds long stories, concerned almost exclusively with his own prowess. In casual conversation no opportunity is lost to boast of or to score a point in his own favor, as often as possible at the expense of some one else. He still addresses most other persons with a certain contempt, or if there is no good opportunity for that, he still discovers a defect of some kind, such as a nasal wart or a loose button, around which the ever continuing monologue is woven. But recently, after leaving the person in question, A usually makes some favorable comment about him.

A's mood, as before, is almost uniformly cheerful, except for occasional angry tantrums. His intellectual output is composed of the old variety of relatively simple products. His limited concern with so-called abstractions is also unaltered. With regard to judgment, A shows the same defects as previously. His judgment about simple things is satisfactory, but he is lost in evaluating matters which require putting many factors together. His sense of humor, or better of comedy, is still on a simple level, and on that level it is good. He appreciates the funny aspects of things perhaps too well and laughs correctly and readily—especially at his own sallies, which are many and often comical.

A's postoperative lack of initiative is unchanged. He still expresses an ardent wish to return to work as a stockbroker and makes no move to carry it out. His time is spent, as before, in going to the barber shop and taking a walk in the morning, attending moving pictures or stage productions in the afternoon and reading the newspaper or sitting with the family after dinner until about 9 o'clock, when he retires. The stereotypy and moderate slowness of thinking which he showed before are evident in unaltered degree.

Four symptoms were previously unclassified—euphoria, use of jargon, compulsions and incontinence. The first two are unchanged. There has been no further rectal incontinence. The status of the compulsions which developed after the operation will be included in a later report. In all the other categories the symptoms previously described are unchanged (Witzelsucht, puerility, distractibility, particularization, aphasia ,perseveration and condensation. A's perseverative trend is illustrated by his frequent use of the phrase "I take exception to" in the examples which follow.) A has added an item to his explanation of the jargon: "It's because I want to say something, and that's the fastest thing I can think of."

The actual jargon words are identical with the old ones. This changelessness is typical of A; his mental content, his manner of thinking and of conducting himself, his human relations and his general approach to life are virtually the same as when he first came under observation seven years ago, at the age of 42. The lack of evidence that there has been any new thought, except of simple order, or any new interest or desire in so long a time is striking and signifies in itself a broad, chronic stereotypy. It appears to be a reflection, again, of loss of the function of synthesizing intellectual units. The continuous combining and recombining of thoughts which normal people experience, as a response either to external changes or to the stimulus of thoughts themselves, are absent. To state it in another way: A has learned nothing since his operation beyond the simplest things which happen around him. From the standpoint of intellect, time has stood still for him. Time, passage, movement have had little meaning

for him. It may not be overspeculative to think that without the accumulation of memories which his frontal cortex once helped him to manufacture and then to store more caudally and without speech A's situation would not be very different from that of a human ancestor. It does not, perhaps, strain the imagination too greatly to think that in A one may have a slight glimmer of the action of the simian mind.

From the standpoint of general behavior, also, the changes since the previous report are few. Possibly there is less force in the manifestations of hostility. He speaks to people as he did before, saying, for example, that they look badly, informing them that he hopes he never sees them again or telling the barber that he knows nothing about cutting hair. Often, however, he does it less positively than before, and this softening is sufficiently marked that the barber considers him to be improved. A's explanation is: "Well, I don't take exception to as many things as I used to because I'm too damned tired of doing it." His family reports him to be somewhat easier to manage, chiefly because he now bathes willingly. A explains this by saying: "In the first place, I know that if I don't take a bath in the morning there will be eighteen people saying 'Did you bathe?' and that gets me sore," and "I took exception to everybody asking me when I went to breakfast, 'Did you have a bath?' And I took exception to having to tell everybody, 'No, I didn't.'" The tying of his shoelaces was formerly a problem, as he consistently refused to perform this function himself. This has been solved by the family's yielding, one of the relatives regularly tying the laces.

A still criticizes his father, but he can be prevented from doing so at length. These jibes usually follow the father's criticism of A.

The most striking of the behavioral changes that have occurred since the previous report is A's treatment of his wife. Formerly he was uniformly inconsiderate and rude to her. Since about a year ago he has spoken to her more courteously and has shown a degree of tender feeling for her. He apologizes when he lapses occasionally into addressing her roughly. Frequently he expresses a desire to have her with him. He is greatly impressed by the knowledge that he has been married for twenty years. When his mother-in-law died A was sympathetic and affectionate with his wife. Although he pays her few attentions on his own initiative (this may be an expression of his general lack of initiative), he responds to her advances more gently and pleasantly than he did formerly.

In illustration of his general puerility, it is of interest that previously A was always embarrassed at affectionate interchanges with his wife in the presence of his parents; he still finds it necessary to make excuses. For example, A beckons her to sit on his lap, at the family gathering after dinner. When she does so, A turns to his parents, saying: "See, I can't help it if she wants to sit on my lap. What can I do?" He kisses and embraces his wife much more often in a gentle, normal way now, but he still refrains from sexual intercourse, the act occurring occasionally without insertion. He continues to masturbate but there is no way to determine the frequency now.

Of special interest is A's lack of appreciation of the gravity of his situation. He still refers to the lobectomy as "a bunk on the head" and shows little knowledge of its having altered him significantly. At most, he admits under pressure that it may have made some slight difference. This symptom occurs occasionally in patients with injuries to various parts of the cortex and has been concerned with such grave disturbances as blindness and deafness. It is present when, as with

A, the patient has ample judgment for appreciation of his state. Sachs [2] has demonstrated that it is not dependent on euphoria; he recorded the cases of 11 patients who had the symptom, only 1 of whom was euphoric. It is possible that the symptom represents agnosia for a function (such as vision, hearing or thinking), similar to agnosia for one's fingers or other parts or even for one whole side of the body (Nielsen [3]).

ABSTRACT OF DISCUSSION

DR. W. F. SCHALLER, San Francisco: I believe that Dr. Brickner's theory of the synthesizing function of the frontal lobe has a rational basis. The symmetry of the frontal lobe and the associative function of the anterior part of the corpus callosum lend support to his idea of bilateral representation. It appears to me that there is here an explanation of the absence of aphasia (as was held by Marie) in undoubted cases of involvement of the left posterior third frontal convolution—Broca's area.

Lobectomies involving Broca's area have been performed by Penfield and by Jefferson, of Queen Square Hospital. Penfield reported a case in which half of Broca's area was removed without resulting aphasia. Of a total of 8 cases of left frontal lobectomy, Jefferson reported 3 in which his diagrams apparently showed involvement of Broca's area, although his article did not specifically state that the patients were right handed.

It appears, then, that with bilateral cortical representation, as postulated by Dr. Brickner, there may not be aphasia unless the common path through the internal capsule is involved, as was demonstrated by Marie.

Von Economo stated that in the development of the human brain there is progressive cerebration; as it is known that the frontal and parietal lobes are those which have been particularly developed as the human brain progressed, this higher, this synthesizing, function is understandable. Von Economo, for instance, expressed the belief that modern music is a development only of recent centuries. He referred to the Bach family as having had five consecutive generations of musicians.

Another point worthy of mention is that brought out by Frederick Tilney, who expressed the belief that many do not use all the reserves of intellect, the location of which includes the frontal lobes. There may, therefore, be a potential area which is not called on in many cases of lobectomy. It would be interesting to know the results of lobectomy in a genius or in a man of outstanding intellectual ability.

Dr. Brickner's presentation fits in well with the address of the chairman of the Section, Dr. S. D. Ingham. There are gradually being formulated more definite concepts of the function of the brain, such as the higher synthesizing action of the frontal lobes and the instinctive reactions and consciousness associated with the diencephalon.

I congratulate Dr. Brickner on his analysis. It is a distinct contribution to knowledge of the function of the brain.

---

2. Sachs, E.: Symptomatology of a Group of Frontal Lobe Lesions, Brain **50**:474, 1927.

3. Nielsen, J. M.: Gerstmann Syndrome: Finger Agnosia, Agraphia, Confusion of Right and Left and Acalculia; Comparison of This Syndrome with Disturbance of the Body Scheme Resulting from Lesions of the Right Side of the Brain, Arch. Neurol. & Psychiat. **39**:536 (March) 1938.

DR. J. M. NIELSEN, Los Angeles: I think that Dr. Brickner will be known as the man who worked out the function of the frontal lobe. That it has not been done before is due partly to want of a good case but largely to lack of a man to do it.

The unilateral cerebral dominance which plays such an enormous role in the functions of the brain plays a far smaller part in the activity of the frontal lobe than in that of the rest of the brain; consequently, if one or the other frontal lobe is removed and one is left intact, there are few symptoms. It has been shown repeatedly that there is no way of telling which is the dominant side until a lesion occurs. In the case of the patient A, no one knows which side was dominant, but it does not make any difference. Both lobes are gone. Now one may form an idea of what the frontal lobes really do.

It has been said that the status of Dr. Brickner's patient is the same as that of a man with dementia paralytica, except that the lesion was made by a surgeon, not by syphilis. The frontal lobes apparently have nothing to do with concepts except to use them. No concepts are stored anterior to the fissure of Rolando, but the part anterior to that fissure makes use of the portion posterior to it; that is what this case shows so well.

DR. WALTER FREEMAN, Washington, D. C.: One of the remarkable things about this patient of Dr. Brickner, who has been studied repeatedly and so well, is the stability which he shows years after his operation. The symptomatology must represent that of frontal lobe deficit. Whether Dr. Brickner's interpretation of the symptomatology of the frontal lobe on the basis of synthesis is valid I do not think one can say, because synthesis is an intellectual process and the phenomena observed have a great emotional component. I think that the emotional aspects of the function of the frontal lobes also have to be taken into consideration. Here is a man previously reasonably well adjusted who became definitely antisocial, with a driving hostility that has persisted all these years.

My associates and I have had some experience with partial lesions of the frontal lobe on both sides in cases in which operation was performed because of certain maladjustments and other emotional difficulties; in a number of instances there has been considerable alleviation of the disharmony of the personality. Several explanations may be advanced. After operation there is reduction of the painful self consciousness that restrains the person from going forward and accomplishing things. If that self consciousness is altogether removed, one can see a magnification of phenomena, such as occurred in Dr. Brickner's case.

We have also observed increased satisfaction with performance, a reduction of that perfectionist spirit that pervades some persons and which in the patients who were operated on was exaggerated and actually interfered with the individual performance. Dr. Brickner spoke of the desire of his patient to go back to work, and yet of his inability or lack of initiative in doing so. One finds that procrastination in patients who have undergone bilateral prefrontal lobectomy is a striking characteristic. They will make plans for the next day and then sit around and watch the sparrows.

The hostility can largely be assigned to the "don't give a damn" attitude, the lack of the painful self consciousness, but in the same category is the absence of a tendency to harp on a system of ideas, the lack of the obsessive thinking that has troubled the patient before. These patients often are better adjusted in some respects. Unilateral operations undoubtedly have little effect, and bilateral representation of cerebral function in relation to the frontal lobe is undoubtedly correct. One might say that the parts posterior to the rolandic fissure are used

in looking backward and the parts anterior in looking forward, the anterior parts of the brain being those that are especially concerned with the executive capacities of the person.

DR. L. H. ZIEGLER, Wauwatosa, Wis.: I have been greatly impressed by this splendid analysis of what happens when a large amount of the frontal portion of the brain is removed. Dr. Brickner's discussion of the effects may be summarized by stating that in this patient considerable poverty of thinking has developed, which is not entirely characteristic of persons who have had frontal brain tissue removed. The patient has no particular insight into his thought processes, which is not necessarily characteristic of patients who have had removal of brain tissue. The emotional inappropriateness and ineffectualness are excellently described; these traits are seen in persons whose brains are intact. The self defensiveness which the patient has shown in a considerable degree is not confined to persons with ablation of the frontal lobe.

There must be conditions which can bring about these changes in behavior when the frontal lobes are intact that make it necessary to think in terms of other mechanisms capable of producing these effects. I do not doubt, however, that the removal of the brain tissue had much to do with the production of altered behavior in the case which Dr. Brickner so ably described.

DR. RICHARD M. BRICKNER, New York: Dr. Schaller's question, in which Dr. Nielsen was also interested, has been debated for many years. The answer appears to be evolving. It relates to possible dominance of one lobe over the other in the function of thinking. I have been able to discover nothing in the literature at all sound which indicates that one lobe has any superiority or dominance over the other in the performance of that function. The best example is Jefferson's report of 8 cases of unilateral frontal lobectomy (the largest series in which the two lobes could be thus contrasted), 6 of which were well studied. In 3 there was left and in 3 right lobectomy. He found no difference between the two groups.

Dr. Nielsen raised another issue concerning dominance. If most of the paired processes, for instance, the muscular functions that I named before, some of the sensory, such as vestibular function, and intellect itself, are bilaterally innervated, what can be the reason that speech is unilaterally represented? Speech is surely as much a paired and generalized function as any. This is a question which should be stressed because its solution may have general implications of unusual value.

Dr. Freeman's remarks about the emotional aspects of the function of the frontal lobe are also pointed. No one is doing more than he to illuminate the matter. It is possible that in the operation that Dr. Freeman and Dr. Watts perform the connection between the thalamus and the frontal cortex is severed so as to deprive the intellect of the feeling tone of which Dr. Ingham spoke before without interfering with the intellectual functions of the frontal cortex. Certainly, patients subjected to this operation, a number of whom I have seen and 2 of whom I have studied rather intensively, show no detectable intellectual deficit.

When Dr. Ziegler asked whether other factors might produce the same effects, I imagine he referred to psychologic factors. I should suppose that they would not. At all events, the aim of those who are studying lobectomy is to see whether the whole problem cannot be stated in psychologic terms.

Technical and Occasional Notes

A SIGN OF FACIAL PALSY

ROBERT WARTENBERG, M.D., SAN FRANCISCO

It is easy to diagnose facial palsy when fully developed, but sometimes extremely difficult to detect it at the beginning. This is true especially when the condition develops slowly—for instance, in cases of a tumor of the angle, disease of the pons or insidiously progressive lesions of the pyramidal tract. Also, it is sometimes difficult to state how completely a previous facial palsy has subsided or to find the last traces of an old facial palsy and thus to prove that such a palsy existed at all. In either instance, the common signs of facial palsy may fail to help, as they are not sufficiently fine.

Especially, all tests of motor function of the facial muscles (strength, rapidity and range of movement) give results that are difficult to appraise. Slight asymmetry of the face or the presence of contractures further increases the difficulties.

More information can sometimes be obtained by testing the reflex activities of the facial muscles, particularly the so-called supraorbital reflex, described in 1901 by McCarthy. This reflex has since been rediscovered several times and given various names (eye reflex by von Bechterew, in 1903; trigeminofacial reflex by Zeni, in 1906; nasopalpebral reflex by Mondino, in 1907, and by Guillain, in 1925, and nose-eye reflex by Simchowitz, in 1927). It is most appropriately called the "glabella reflex," as the glabella is the area from which this reflex is best elicited. Slight percussion of the glabella with a percussion hammer provokes contraction of both orbicularis oculi muscles with resultant blinking of the eyes. On the side on which facial palsy has occurred, the contraction of this muscle is much weaker. Any difference between the two sides must be regarded as of pathologic significance. In cases of complete facial palsy no contraction occurs at all. This reflex is constant and persistent. I found it preserved even in a case of congenital aplasia of the first trigeminal branch, in the region of which there was complete anesthesia of the skin for all kind of sensibility. The reflex becomes diminished or even absent early in the course of slowly progressive peripheral facial palsy, such as may be due to a cerebellar or an intrapontile tumor or a tumor of the cerebellopontile angle. It may thus constitute the first sign of forthcoming palsy of the seventh nerve. When facial palsy is subsiding this reflex reappears soon; it may then even become exaggerated on the side previously affected.

From the Department of Neurology of the Division of Medicine, the University of California Medical School.

A still more dependable and sensitive sign of even the slightest degree of facial palsy was described by Bergara [1] and, independently, by me.[2] We differed only in the technic of eliciting the sign.

My technic is as follows: If when a normal person is closing his eyes one exerts slight upward pressure on the upper lids with the ball of the thumb one feels a fine vibration in the upper lids. As the eye is closing, one feels distinctly a great number of very fine contractions, occurring in rapid succession, which make up the sustained contraction of the orbicularis oculi muscle. This is easily explained physiologically by the fact that every contraction of a muscle is practically tetanus.

The vibration of a muscle can even be heard. If one lies on one side in bed and presses the head against the pillow, one may hear on closing the eyes a fine buzzing sound produced by the fine jerky oscillations of the orbicularis oculi muscle, which are transmitted to the ear by the pillow. In the same manner, contractions of the masseter muscle or of the muscles of the arm and hand may be heard.

In testing a patient, with the ball of the thumb placed on, or slightly above, the upper lid, the vibration can be felt best when the patient uses a slight degree of effort to close the eyes. In every case the optimum of vibration can be found by having the patient vary the degree of effort expended. The degree of vibration felt does not parallel the strength of the contraction; in very strong contractions vibration may not be evident at all. It has been felt even in a semiconscious patient. It is essential to keep in mind that by this method one tests not the strength of the orbicularis oculi muscle but only the vibration of the upper lid.

The vibration felt by the palpating finger is equal on the two sides in the normal person and is absent in the patient with complete facial palsy. In a case of facial palsy of slight degree, either as a vestige of complete involvement or as the first stage of facial palsy, marked diminution in the vibration of the upper lid can be felt; the oscillations of the muscle are less vigorous, less frequent and less extensive. Again and again, one is amazed to note how greatly this vibration is diminished even when the subject is able to close his eyes with considerable force. In the course of recovery from facial palsy, the vibration returns and assumes a normal character extremely slowly and late. Herein lies the diagnostic importance of this test. Even though by inspection and electrical examination no definite remnant of the old facial palsy can be revealed, and though the strength of the orbicularis oculi and other facial muscles has become essentially normal, one can feel on the side formerly affected marked diminution of vibration. This is particularly striking in cases of old facial palsy with contractures and coordinated movements on the side formerly affected in which, at first glance, the opposite side seems to have been affected by the palsy. Here a test of the vibration of the upper lid reveals at once the real state. Facial palsies which originated as long as twenty years before and which had completely or nearly completely disappeared, have been detected,

1. Bergara, C.: Un nuevo signo de parálisis facial, Rev. de especialid. **1**:556, 1929.

2. Wartenberg, R.: Ein Symptom der Fazialislähmung, Klin. Wchnschr. **9**: 1587 (Aug. 23) 1930; Deutsche Ztschr. f. Nervenh. **116**:144, 1930.

in many instances exclusively, by this test. In cases of slowly developing facial palsies the test reveals the condition at its beginning, even when all other signs and symptoms fail to help. Thus, decrease in vibration seems to be both the last and the first sign of facial palsy.

By use of the symballophone designed by Dr. W. J. Kerr,[3] one can easily hear on both sides the sounds produced by the vibration occurring when the eyes are closing and can compare their character. One merely places the bulbs over the eyelids or on the external corners of the eyes and, having asked the patient to close his eyes, exerts a slight pressure upward or sideward, depending on the position of the bulb. The examination by symballophone supplements to a gratifying degree the results obtained by palpation.

In physiologic experiments carried out by Dr. H. Rein, in Freiburg, Germany, on a patient of mine with facial palsy of long standing, it was graphically demonstrated that on the affected side the number and amplitude of oscillations in the orbicularis oculi muscle while in action were markedly diminished.

I have the definite impression, based on experience of over ten years, that this test is the finest and most dependable sign of facial palsy, even of the slightest degree; it may be depended on when other signs or symptoms are absent. It has been repeatedly found that in cases of subsiding facial palsy the glabellar reflex had become normal but the vibration of the upper lid was still diminished. In some cases in which the condition was difficult to diagnose—for instance, tumor of the angle, disease of the pons and old facial palsies with contractures—the diagnosis of an oncoming or old facial palsy has been based exclusively on this sign, and it has never proved disappointing.

The sign is so reliable that if the vibrations of the upper lid as perceptible by palpation are equal on the two sides one can definitely state either that facial palsy has never existed or that it has subsided completely.

The sign is present with facial palsy of central as well as of peripheral type, being more pronounced in the latter. For the differential diagnosis of central peripheral palsy it cannot be used.

Neurologists formerly paid much attention to the so-called Rosenbach phenomenon: a visible, fine, rapid tremor of the upper lid on closing the eyes (*Lidflattern* of the Germans), which was observed in cases of exophthalmic goiter and of general nervous hyperirritability. This tremor can be detected more definitely by palpating the upper lid, as already described. In neuropathic states, exophthalmic goiter, alcoholism and extrapyramidal diseases one can find by palpation a marked increase of this tremor, which may be useful in diagnosis.

SUMMARY

Decrease of vibration in the upper lid felt by the examiner's palpating finger, which exerts upward pressure on the upper eyelid as the patient closes the eye, constitutes the finest and most reliable sign of facial palsy.

3. Kerr, W. J.; Althausen, T. L.; Bassett, A. M., and Goldman, M. J.: The Symballophone: A Modified Stethoscope for the Lateralization and Comparison of Sounds, Tr. A. Am. Physicians **52**:92, 1937; Am. Heart J. **14**:594 (Nov.) 1937.

News and Comment

MEDICAL SOCIETY OF ST. ELIZABETH'S HOSPITAL

The Medical Society of St. Elizabeth's Hospital will hold its second annual meeting in Washington, D. C., on April 14, 1939. Members of the society will be luncheon guests of Dr. Winfred Overholser, superintendent, on that date. The afternoon will be devoted to the presentation of papers describing research interests of members of the society; in the evening there will be a dinner at a Washington hotel. Dr. C. Macfie Campbell, director of the Boston Psychopathic Hospital and professor of psychiatry at the Harvard University Medical School, and Dr. Riley H. Guthrie, newly appointed first assistant physician at St. Elizabeth's Hospital, will be guests of the society. The chairman of arrangements is Dr. S. Katzenelbogen, St. Elizabeth's Hospital, Washington, D. C., from whom further details may be obtained.

POSTGRADUATE COURSE AT MENNINGER CLINIC

For the fifth consecutive year the psychiatric staff of the Menninger Clinic, Topeka, Kan., offers a week's postgraduate course in Neuropsychiatry in General Practice, April 17-22, 1939. This practical presentation of dynamic psychiatry through lectures and case presentations has been attended by physicians from nineteen states in the past four years. Enrolment is limited to thirty. Address inquiries to Dr. Robert P. Knight, chairman, Menninger Sanitarium, Topeka, Kan.

Obituaries

HUGH TALBOT PATRICK, M.D.
1860-1939

Dr. Hugh Talbot Patrick, who died on Jan. 5, 1939, was born at New Philadelphia, Ohio, May 11, 1860, the son of Abraham Westfall and Mary West (Talbot) Patrick. His grandfather came from Belfast, Ireland, in 1817 and settled first in Philadelphia and later in New Philadelphia, Ohio, where he established the "Tuscarawas Chronicle," the first newspaper in the county and one of the first in eastern Ohio, and was county auditor, county recorder, United States land agent and judge of the court of common pleas. His father received many honors from the state. He was elected prosecuting attorney in 1858; in 1867 he became probate judge, relinquishing his office to go to the Ohio legislature as senator. In 1900 he received the endorsement of the Ohio delegation for Vice President of the United States, but he did not permit his name to go before the convention. Known lovingly as "Uncle Abe" to thousands in Ohio and beyond the border of the state, it was said of him: "His convictions are strong on all subjects regarding which he has reached a definite conclusion, but he is nevertheless broad-minded and liberal, charitable in his judgments and faithful to his friends." How this was mirrored in his son!

Dr. Patrick attended the University of Wooster, from 1878 to 1880, and was graduated with the degree of Doctor of Medicine from the Bellevue Hospital Medical College (New York University) in 1884. After a year and a half as intern at the Randall's Island Hospital, New York city, he began practice in Chicago in 1886.

From 1891 to 1894 he took postgraduate work in nervous and mental diseases at the principal medical centers of Germany, France and England, and since that time had a continuous friendly and scholarly contact with the leaders of English and continental European neurology. For a time he was professor of nervous and mental diseases at the Chicago Policlinic. He was appointed to the faculty of the Northwestern University Medical School in 1895, with the rank of instructor. In 1898 he was appointed associate professor, in 1902 professor and in 1919 emeritus professor, of nervous and mental diseases. He was a counselor of the medical school. He was attending neurologist to the Wesley Memorial Hospital, the Passavant Memorial Hospital and the Peoples and Henrotin Memorial Hospitals and consulting neurologist to St. Anthony Hospital and the Illinois Charitable Eye and Ear Infirmary.

He was a founder of the Chicago Neurological Society, its first secretary and then twice its president. He was a member of: the American Neurological Association, serving twice as its vice president and as its president in 1907; the Institute of Medicine of Chicago, of which he was once president; the American Medical Association, acting as secretary and chairman of its Section on Nervous and Mental Diseases; the Chicago Medical Society, of which he was a trustee; the Mississippi Valley Medical Association, of which he was once president; the Illinois State Medical Society; the Chicago Pathological Society; the Chicago Society of Internal Medicine; the Central Neuropsychiatric Association; the Chicago Academy of Medicine, and the Association for Research in Nervous and Mental Diseases; he was foreign corresponding member of the Société de neurologie de Paris.

He was the author of numerous scientific treatises, the founder of the ARCHIVES OF NEUROLOGY AND PSYCHIATRY and its chief editor. He was a member of the editorial board of the *Journal of Nervous and Mental Diseases.* He was the first to receive the honor of a dedicated issue of the ARCHIVES OF NEUROLOGY AND PSYCHIATRY, in 1936. For many years he was an editor of the "Year Book of Neurology and Psychiatry."

He served his country during the World War as consulting neurologist at Fort Benjamin, Ind.; Camps Zachary Taylor, Ky., and Shelby, Miss.; East Norfolk, Mass., and Fort Sheridan, Ill.

During the last eight years of his life he retired from active practice and developed special interest in biography and the historical aspects of neurology.

He was an honorary member of Alpha Omega Alpha. The honorary degree of Doctor of Science was conferred on him by Northwestern University in 1927. He had the distinguished honor of being elected to the Legion of Honor of France, with the rank of Chevalier.

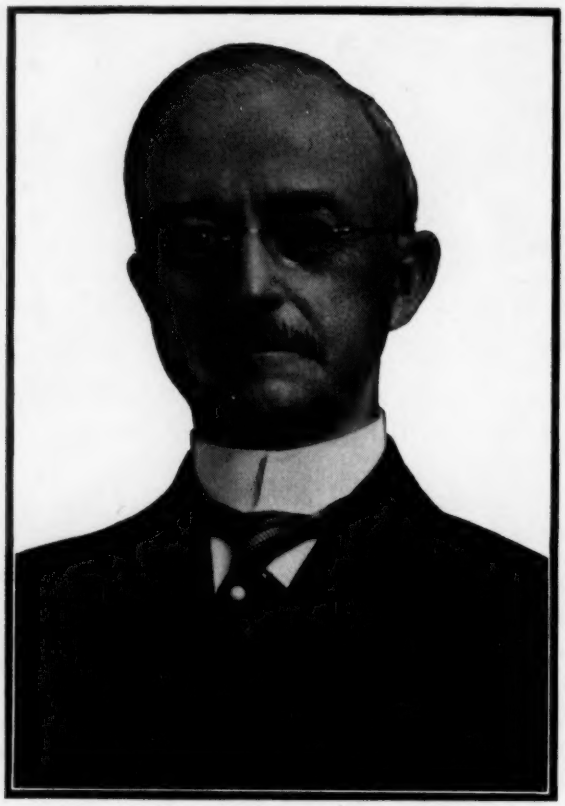
He was married on April 28, 1896, to Fannie E. (deceased), daughter of Joseph E. Gary, for over forty years judge of the Superior Court of Chicago. They had three children, Talbot, Catherine and Elizabeth Patrick (deceased).

This brief biographic recital gives only a feeble idea of the character, the brilliance, the color and the kinetic force of the man who was Patrick.

When the honorary degree of Doctor of Science was conferred on him by Northwestern University, in 1927, the *causa honoris* read as follows:

> Hugh Talbot Patrick, distinguished neurologist of international fame; profound student and stimulating teacher; clinical investigator of great achievement; inspirer of youth; Chevalier de la Legion de l'Honneur of France; servant of his country in time of need; Emeritus Professor in this University and a Counsellor of Medicine; a learned, kindly physician. . . .

At a time when in the Middle West the practice of neurology was included in that of internal medicine and sufferers from nervous disease were classified as freaks, Dr. Patrick began the practice of his specialty only after extensive preparation. As Sachs said, Patrick was one of those who "built carefully, keeping a solid foundation of facts and rearing clinical neurology on the basis of neuro-anatomy and neuro-pathology. [He] kept his feet on the ground and . . . stood for pains-



HUGH TALBOT PATRICK, M.D.
1860-1939

taking scientific investigation, submitting all theoretical speculation and fanciful doctrines to the test of cold logic." Because of this he was responsible, to a great degree, for the development in the Middle West of the art and practice of neurology.

In 1898 he was one of the founders of the Chicago Neurological Society. It is significant that in the earlier years on the roster of membership appeared many names of the prominent specialists in internal

medicine, only later to disappear as the specialty of neurology became recognized. At first, at many of the meetings only six to ten members were present, perhaps four of them presenting papers and all joining in the discussion. Among these, Patrick contributed liberally.

Soon, in the American Neurological Association he was one of the group that included Starr, Sachs, Dercum, Spiller, Dana, Collins, Peterson, Adolf Meyer, Tilney and Cushing, and he joined with them in contributions to contemporary neurology. By means of this association he was instrumental in effecting the recognition of neurology in the Middle West.

Most important of all were his services in the foundation of the ARCHIVES OF NEUROLOGY AND PSYCHIATRY, making it a leading, if not the leading, publication in its field in the world. He was active in organizing support for this periodical and became its first editor. As editor of the ARCHIVES he was instrumental in making it reflect the progress of American medicine in the fields of neurology and psychiatry and in placing them on the highest scientific level.

To illustrate his grasp of the entire neuropsychiatric field, mention may be made of a few of the subjects of his literary contributions: degeneration following complete compression of the spinal cord; course and destination of Gowers' tract; the motor neuron; arteriosclerosis of the nervous system; cyst of the cerebellum; tumor of the pituitary body; cyst of the pituitary body; apoplexy; hereditary cerebellar ataxia; amaurotic family idiocy; chronic progressive hemiplegia; cerebral syphilis and dementia paralytica; locomotor ataxia; multiple sclerosis; paralysis agitans; chorea and tic; epidemic encephalitis; epilepsy; trifacial neuralgia, especially his success in the palliation of pain; muscular atrophy; multiple neuritis; facial spasm; cervical rib; brachial neuritis; sciatica; facial diplegia; intermittent claudication; hypnotism; hysteria; traumatic neurosis; headache; reflex neurosis; ambulatory automatism; imperative conceptions; disorders of sleep; war neurosis; the chronic invalid; fear; the patient himself.

As a clinical investigator he contributed pictures of unusual clarity in the differentiation of diseases. Among these may be mentioned his descriptions of hysteria, traumatic neurosis and phobias; the remarkable description of the pain in trifacial neuralgia, and the studies on headaches, tics and chorea, brachial neuritis and sciatica, chronic progressive hemiplegia and unilateral paralysis agitans without tremor, *débutant* attacks of epilepsy and, particularly, the patient himself.

Although decrying short cuts, his aptitude for effective description is reflected by such titles as "Seven One Minute Points on Syphilis of the Nervous System."

As a teacher he eliminated all irrelevant, immaterial, redundant and controversial material. He avoided such pedagogic sins as lead to waste of time by overattention to details or such exposition of his own learning as might be beyond the grasp of the student. He possessed the happy faculty not only of seeing that which alone was significant but of dramatically and illuminatingly reflecting it for the student to see and remember. Above all, he was practical and was one of the first to teach how to study and treat the patient himself. He was noted for obtaining an orderly precise history, elicited by intelligent questioning, guided by clinical sense, completeness of examination, insistence on accurate measurements and recording of facts and a capacity for clearly determining the significance and correlation of symptoms and differentiation of integrated signs.

To the university he brought his valuable services not only as a clinician and teacher but as a wise counselor and guide and example to all in his greatness of intellectual honesty.

To those of us who were his assistants the thought must have come of how often in referring to us as assistants his eyes must have twinkled. In retrospect, one wonders how he could have functioned as well as he did with us as impediments. Clearly, under the guise of employing us he actually assumed a preceptorship over successive young students, to whom he gave so generously of his experience and example.

He was of impeccable integrity and expected it in others. Although he could not suffer fools gladly, he could forgive stupidity, obtuseness or dulness, but a person in whom he detected the slightest lapse from honor became anathema. He was bold and courageous. What might have been a disability to others was not even a blemish to him. But he was never quixotic, never the crusader. He was brilliant, but with neither glare nor glitter. His was a keen, soft, yet penetrating brilliance, and it was pleasant to be within its radiance. He was tactful, but when occasion warranted he could deliver a rapier-like thrust with a single word or sentence. He was gifted as a natural leader of men and thought. He was steadfast, incapable of changing his colors, chameleon like, to further his or anybody else's purposes. He was learned, but not unworldly; the sage, not the seer; a thinker, but never the visionary. He was of infinite complexity of mind, but of extreme simplicity of taste and manner. He was a strict disciplinarian, yet never the martinet, never imperious and with no exaggerated sense of his own infallibility.

He was quick of perception, but never too quick for the inclusion of logic and reason. He had a felicitous gift of wit and humor, yet he was seldom caustic. As is so common in men of distinction, he deprecated oral expression of praise; yet he was by no means insensitive to good work, to which he would respond with a glowing expression, a twinkle

of the eye or a certain chuckle reserved for such occasions, which one with a little experience could recognize. He made unceasing and unyielding demands of meticulousness, carefulness, exactness and accuracy, but he demanded as much of himself as he did of others.

His writing was characterized by simplicity—the simplicity of the consummate artist, who with seeming unobtrusive ease succeeds in accomplishments which may be the delight or the despair of lesser men. Beneath the point of his pen there converged lush, clear thinking, felicity of word and phrase, masterful construction.

The tribute paid by Dr. Bassoe, speaking for Dr. Patrick's former assistants on the occasion of the dedication of a special number of the ARCHIVES in November 1936, may appropriately be repeated here:

"We, your former assistants and the associates of your former assistants, are workers in the field of neurology and psychiatry largely through the stimulus you gave us in our formative years. We eagerly sought the opportunity to be inducted into this field by you. We knew that there was little scientific neurology in Chicago before you blazed the way. What the late Christian Fenger did to give young physicians in the Cook County Hospital and the medical schools of Chicago a vision of scientific pathology and surgery you did in your field. Contact with you by students in classrooms and dispensaries and by physicians in hospitals and sick-rooms and in your office was a steady source of fruitful stimulation to them. We who came in closer contact with you not only were inspired by your teaching and your shining example as a clinician but learned to love you for your kindliness and to admire you for your sterling character and your straightforwardness in dealing with people and problems."

LEWIS J. POLLOCK, M.D.
PETER BASSOE, M.D.
RALPH HAMILL, M.D.
N. LIONEL BLITZSTEN, M.D.
HARRY PASKIND, M.D.

The following resolutions were passed at the March meeting of the Chicago Neurological Society:

"Whereas, on Jan. 5, 1939, Dr. Hugh Talbot Patrick departed this life and

"Whereas, he was a founder of the Chicago Neurological Society, active in the direction of its early development, contributed to its full growth and was beloved and admired by its members and

"Whereas, Dr. Patrick was not only an eminent neurologist of international fame, a learned kindly physician, inspirer of youth, a faithful friend to his patients, his students, his assistants and to us, but was a 'good and faithful servant'

"RESOLVED, that in the passing away of Dr. Patrick, the Chicago Neurological Society, the medical profession and international neuro-psychiatry have suffered a great loss but that we are bigger and better for his having lived and labored and be it

"RESOLVED, that we extend to his bereaved family our profound sympathy, that these resolutions and memorial be spread upon our records and a copy of them sent to the family of our late associate and to the ARCHIVES OF NEUROLOGY AND PSYCHIATRY."

Lewis J. Pollock
Peter Bassoe
Ralph Hamill
N. Lionel Blitzsten
Harry Paskind
Committee

Abstracts from Current Literature

Physiology and Biochemistry

RESPONSES OF MUSCLES OF THE SQUID TO REPETITIVE STIMULATION OF THE GIANT NERVE FIBERS. C. L. PROSSER and J. Z. YOUNG, Biol. Bull. **73**:237, 1937.

With increasing frequency of stimulation of a giant nerve fiber in the squid, Loligo pealii, the increase in the tension developed by the circular muscle fibers of the mantle is only from 5 to 10 per cent over the range of incomplete relaxation. The absence of any increased response at higher frequencies shows that in the fresh muscle a single nerve impulse is capable of activating every muscle fiber which it reaches. The isolated muscle readily becomes fatigued when stimulated at high frequency, and thereafter greater tension is produced at the higher rates.

COBB, Boston.

CHEMICAL TOPOGRAPHY OF THE BRAIN. LOWELL O. RANDALL, J. Biol. Chem. **124**:481, 1938.

In an attempt to relate function of the brain to chemical composition, a systematic examination of the chemical constituents of 23 brains from normal and psychotic subjects was made. The mean water content was higher in the areas of gray matter, the frontal and parietal cortex and the caudate nucleus, than in the areas of white matter, the corona radiata and the white matter of the frontal and parietal lobes, while the brain stem and thalamus had intermediate values. The values for the various lipid constituents—total lipid, acetone soluble lipid, total cholesterol, free cholesterol, phospholipid, phospholipid fatty acid, lipoid phosphorus and lipid nitrogen—were higher in the white areas than in the gray areas and were intermediate in the mixed areas. The iodine number of the phospholipid fatty acids was higher in the gray than in the white tissues. The amounts of acid-soluble nitrogen, creatine, inorganic phosphorus, protein nitrogen and total nitrogen were higher in the gray than in the white tissue and were intermediate in the mixed tissues. Only acid-soluble phosphorus and ester phosphorus had a similar distribution over all the areas.

PAGE, Indianapolis.

HYPERTHYROIDISM AND BRAIN OXIDATIONS. ROBERT A. COHEN and R. W. GERARD, J. Cell. & Comp. Physiol. **10**:223 (Aug. 20) 1937.

The objective of this study was the demonstration of the steps in the oxidation sequence which are hastened by the thyroid hormone and the cell enzymes activated by it. The brains of normal and those of hyperthyroid rats were compared for their ability to oxidize various substrates, and the relative effects of specific respiratory inhibitors were determined.

The brain of a hyperthyroid animal had a distinctly increased respiratory rate. Thyroxinized brain burned substrates with oxygen at a rate 30 per cent or more greater than normal. The catalytic activity, furthermore, was not increased in similar proportions for all oxidations, but was specific for certain substrates. Substances which occur in the sequence of carbohydrate oxidation or glycolysis were more rapidly oxidized by the brains of hyperthyroid than by those of normal animals. Analysis of the respiratory changes indicated that the absolute concentration of various enzyme systems is greater in the brains of hyperthyroid than in those of normal rats, and that certain dehydrogenases are increased relatively more than oxidases.

CHORNYAK, Pittsburgh.

FUNCTIONAL ACTIVITY AND p_H OF THE CEREBRAL CORTEX. J. G. DUSSER DE BARENNE, W. S. MCCULLOCH and L. F. NIMS, J. Cell. & Comp. Physiol. **10**:277 (Oct. 20) 1937.

The authors report on the relations of the p_H of the cortex to its activity and excitability under various experimental conditions, including electrical stimulation. Hyperventilation or intravenous injection of sodum bicarbonate in the curarized animal during artificial respiration results in a marked shift of the cortex to the "alkaline" side. This change is accompanied by an increase in its electrical activity. Hypoventilation or intravenous injection of a dilute acid in the curarized animal during artificial respiration results in a marked shift of the cortex to the "acid" side. This change is accompanied by a decrease in the electrical activity of the cortex. After-discharge in the cerebral cortex results in a decreased p_H at the site of the discharge, whether this is induced electrically by direct electrical stimulation of the focus or neurally by a disturbance propagated from a distance.

CHORNYAK, Pittsburgh.

BRAIN POTENTIALS AND VOLUNTARY MUSCLE ACTIVITY IN MAN. H. H. JASPER and H. L. ANDREWS, J. Neurophysiol. **1**:87 (March) 1938.

Jasper and Andrews investigated the relation between cortical potential rhythms as recorded through the unopened skull and tension rhythms in the musculature of the forearm by means of simultaneous records of finger tremors, muscle action potentials and cortical potentials in normal subjects and in patients with paralysis agitans and petit mal epilepsy. The frequency of normal tremor movements was found to correspond closely with that of potential rhythms from the region of the cortex anterior to the central fissure, the major rhythm being about 10 per second. During normal sleep the tremor rhythms showed changes which paralleled the changes in potential rhythm. Sensory stimulation may depress the tremor and the cortical potentials, or it may cause dissociation of cortical potentials and tremor rhythm. This suggests a relationship between cortical and subcortical centers in the normal subject at rest which is reflected in the grouping of discharges reaching the final common pathway, but this relation may be disturbed by sensory stimulation. The tremor did not appear in the cortical potential rhythms in cases of unilateral paralysis agitans, but appeared occasionally in cases of bilateral involvement. The authors conclude that the normal functional integration of cortical and subcortical motor centers is interrupted by only a moderate or unilateral involvement of the striatopallidal motor system. More extensive bilateral involvement may produce subcortical activity, which occasionally takes over the control of cortical rhythms. Cortical seizure waves in epileptic patients may be associated with corresponding bursts of muscle potentials.

ALPERS, Philadelphia.

THE DISTRIBUTION OF THE ALPHA RHYTHM OVER THE CEREBRAL CORTEX OF NORMAL MAN. MORTON A. RUBIN, J. Neurophysiol. **1**:313 (July) 1938.

Electroencephalograms were obtained from 17 subjects to determine the distribution of the alpha rhythm over the cerebral cortex and to evaluate the use of monopolar and bipolar recording for this purpose. The following results were obtained. Monopolar recording from electrodes on the scalp gives a truer representation of the amount of activity of 10 per second frequency ("per cent time alpha") in the cerebral cortex than does bipolar recording. There were at least two regions of the cortex which showed maxima of α activity, usually some part of the occipital and the frontal lobe. The curve describing the distribution of "per cent time alpha" in the occipital lobe was stable and could be reproduced even over long periods. The distribution curve for the frontal lobe, however, was extremely variable, fluctuating over short intervals (one-half hour) and from day to day. The bursts of α waves from the two cerebral hemispheres of some

persons were least synchronized in the back of the head, more perfect unison between the rhythms of the two sides being obtained the more anteriorly one recorded along the head. The bursts of α activity and the "silent" periods between them did not occur simultaneously in the occipital and in the frontal lobes. Often the frequency of the α waves in the frontal lobes was slower than that in the occipital lobes; waves of both frequencies, however, were obliterated when the subject opened his eyes. The evidence reported here indicates that the α rhythms of the two hemispheres are relatively independent of each other and that the α rhythm may arise in all regions of the cerebral cortex.

ALPERS, Philadelphia.

THE INTERPRETATION OF POTENTIAL CHANGES IN THE SPINAL CORD. DONALD H. BARRON and BRYAN H. C. MATTHEWS, J. Physiol. **92**:276, 1938.

With leads on a dorsal nerve root, reflex stimulation results in the recording of slow potential changes in which the lead proximal to the cord is negative. These are not accompanied by rapid changes attributable to spike potentials. They may be summated or occluded, but neither facilitation nor inhibition was observed. Similar slow potential changes were recorded from ventral roots. Here, too, the proximal electrode was negative. These slow potentials precede discharge of impulses, the spike potentials rising from the slow potential background. The frequency of discharge of impulses is related to the level and rise of the slow potential. Unlike the potentials of the dorsal root, those of the ventral root may be reduced by stimuli which inhibit discharge of impulses. Antidromic volleys via the ventral roots produce only a small potential change and do not greatly affect the slow potential. Such a volley resets the rhythm of discharge of the motor units. The motor neuron is compared to a sense organ. The slow potentials are interpreted as electrotonic spread from the cord. They are discussed in relation to the membrane theory.

McCOUCH, Philadelphia.

CHOLINESTERASE CONTENT OF THE BLOOD IN MYASTHENIA AND PARKINSON'S DISEASE. E. PICKLER, Arch. f. Psychiat. **107**:669 (Dec.) 1937.

Pickler concludes that prostigmine inhibits the ability of the blood to destroy acetylcholine both in normal persons and in persons with myasthenia gravis. In the blood of myasthenic persons the capacity for breaking up acetylcholine is lowered, but apparently the production of this substance is still further diminished. Prostigmine produces its effect by inhibiting the function of the esterases. In Parkinson's disease acetylcholine cannot be demonstrated either in the blood or in the cerebrospinal fluid. After exercise, patients with parkinsonism show a demonstrable increase in the esterase content of the blood.

W. MALAMUD, Iowa City.

Neuropathology

ACUTE ENCEPHALOMYELITIS FOLLOWING GERMAN MEASLES. CHARLES DAVISON and LOUIS FRIEDFELD, Am. J. Dis. Child. **55**:496 (March) 1938.

Davison and Friedfeld report 6 cases of encephalomyelitis following rubella, in 3 of which the outcome was fatal. The course of the exanthem gave no warning of the complications which were to follow clearing of the rash. These occurred over a period of six days, with sudden onset of headache, irritability, vertigo or vomiting, occasional convulsions or coma. There was multiplicity of signs and symptoms indicating diffuse encephalomyelitis. There was only a moderate constitutional reaction. The spinal fluid showed an increase of cells, averaging 40 lymphocytes per cubic millimeter. The encephalomyelitis apparently was acute and self limited and resulted either in complete recovery without sequelae or in

death in a few days. In the case in which histopathologic study was made, there were slight meningitis, some involvement of ganglion cells and perivascular infiltration of the gray and white matter of the cortex, the brachium pontis, the superior cerebellar peduncle, the dentate nuclei, the cerebellum and the brain stem.

WAGGONER, Ann Arbor, Mich.

HYPERINSULINISM AND CEREBRAL CHANGES. N. MALAMUD and L. C. GROSH JR., Arch. Int. Med. **61**:579 (April) 1938.

Malamud and Grosh report the case of a woman aged 30 who had had hypoglycemic reactions for six years. Fainting spells, which were relieved by ingestion of food or sweets, gradually merged into convulsive attacks and a concomitant change in the mental status, characterized by irritability, resistiveness, impulsiveness and, finally, gradual but progressive deterioration. At necropsy an encapsulated adenoma of the islet cells was seen. The brain weighed 1,125 Gm. The leptomeninges were thin and moderately congested. The cerebral cortex showed generalized parenchymatous degeneration, most pronounced in the left hemisphere and affecting chiefly layers 3 and 5. In some areas the degeneration extended also into layers 2 and 6, whereas the fourth layer was usually well preserved. In the first layer there was considerable gliosis. The white matter was essentially normal, with only slight rarefaction in the myelin sheaths and moderate increase in the number of glial fibers.

BECK, Buffalo.

PATHOLOGY OF COCCIDIOIDAL GRANULOMA OF CENTRAL NERVOUS SYSTEM AND ITS ENVELOPES. CYRIL B. COURVILLE and KENNETH H. ABBOTT, Bull. Los Angeles Neurol. Soc. **3**:27 (March) 1938.

Courville and Abbott contribute a general survey of 19 cases of coccidioidal lesions of the central nervous system and meninges. The causative organism, Coccidioides immitis, is a plant parasite related to the molds and has a spherical granular body, with a clear refractile membrane. The diameter varies from 5 to 50 microns, and the organism is easily seen lying either in granulation tissue or in giant cells. The portal of entry is through the skin, with ulceration, or through the lungs, with production of mild pneumonia. Widespread dissemination occurs through the blood stream. The nervous system is involved in 25 per cent of cases in which there are metastases. The tissue reaction is granulomatous, closely resembling the tuberculous form except for the tendency to liquefaction necrosis rather than caseation.

Neurologic lesions may occur as: (1) extradural cranial or spinal abscess, (2) leptomeningitis or (3) involvement of the nerve tissue proper. Small punched-out areas occur in the skull and may lead to perforation or subpericranial abscesses, but not to diffuse osteomyelitis. Similar erosions may occur in one or more vertebrae and may produce a deformity similar to that seen in tuberculosis. The spinal cord is sometimes compressed by an extradural exudate or, rarely, by vertebral collapse. The leptomeningeal involvement assumes various forms. Yellowish gray tubercles are seen predominantly in the area of distribution of the middle cerebral artery and are similar to those due to tuberculosis, except that they are likely to be larger and more flattened and irregular. Diffuse granulation tissue in the form of a grayish yellow exudate may fill the fissures, cisterns and spaces at the base of the brain and may be so profuse as to obscure the underlying structures. Similar diffuse granulation may surround the spinal cord and distend the spinal subarachnoid space. A so-called intracisternal abscess is unusual and consists of liquefied masses of granulation tissue. In the same way, localized granulomas may occur in the subarachnoid space. The spinal fluid usually shows elevated pressure, increased globulin, somewhat decreased sugar content and pleocytosis,

the number of lymphocytes varying from 11 to 1,200 per cubic millimeter. Eosinophilia may be present in the spinal fluid, and polymorphonuclear cells may be numerous, being as high as 100 per cent in mixed infections. The colloidal benzoin curve is inconstantly elevated in the first or middle zones. Organisms are isolated rarely and in acute forms and may be recovered by inoculation of guinea pigs. Clinically, the meningeal forms are divisible into acute and chronic meningitis. In only 2 of the 19 cases studied by Courville and Abbott did granulomas occur in the nerve tissues proper, once in the cerebral cortex and once in the thalamus. These lesions were rather sharply delineated and irregular and presented a typical granulomatous appearance.

MACKAY, Chicago.

HUNTINGTON'S CHOREA AND LUETIC MENINGO-ENCEPHALITIS. THEODORE T. STONE and E. I. FALSTEIN, J. Nerv. & Ment. Dis. **87**:450 (April) 1938.

Clinically, the patient described by Stone and Falstein presented manifestations typical of Huntington's chorea. The family history on the mother's side showed heavy tainting with Huntington's chorea. The Wassermann reactions of the blood and spinal fluid were positive. Death followed advancing dementia and loss of weight, at the age of 39.

Complete pathologic examination of the brain was not made, since the basal ganglia were missing. There was chronic thickening of the pia-arachnoid over the whole brain, including the septums, with heavy infiltration with large and small round cells, plasma cells and macrophages. The cerebral cortex was atrophied, and the cortical ganglion cells showed chronic degeneration in all areas, with architectonic disorder. There was greatly increased vascularity, with perivascular infiltration with plasma cells throughout the cortex. Similar changes were present in the cerebellum, with cellular infiltration, atrophy and distortion of the Purkinje cells and increased vascularity. There was no marked disturbance of myelin in the white matter. Marked proliferation of fibrous and protoplasmic glia cells was observed in all regions of the cortex. Stone and Falstein state that though this case was clinically one of Huntington's chorea, there were pathologic evidences only of dementia paralytica. The basal ganglia, however, were not examined. Similar association of Huntington's chorea with the pathologic features of dementia paralytica has been reported frequently. Such a coexistence of the two disorders is not remarkable, but in this event one should have pathologic evidence of Huntington's chorea.

MACKAY, Chicago.

SOME PROBLEMS OF HISTOLOGICAL DIAGNOSIS AND INTERPRETATION OF CIRCULATORY DISTURBANCES IN THE BRAIN. A. MEYER, J. Ment. Sc. **84**:97 (Jan.) 1938.

Meyer calls attention to the occurrence of special areas of anemic necrosis of the gray matter without evidence of involvement of the cerebral vessels. Some vascular lesions may follow the functional disturbance of organically healthy vessels. Meyer refers especially to angiospasm, prestasis and stasis. Tissue changes were considered previously to be due either to the rupture of vessels or miliary aneurysms with subsequent hemorrhage or to the obliteration of vessels by thrombosis or endarteritis. Meyer cites records of postmortem examinations in which typical hemorrhages and areas of softening without rupture or obliteration of blood vessels were observed. Certain regions of the brain are especially vulnerable to disturbances of blood supply. Such regions are the cornu ammonis, the Purkinje cell layer of the cerebellum and the pallidal system. Deprivation of oxygen is an important factor in the production of these circulatory disturbances. Meyer believes that this is closely related to the enzymes activating oxygen consumption, especially vitamins B and C.

KASANIN, Chicago.

CEREBELLAR SYNDROME IN AN ADULT WITH MALFORMATION OF THE CEREBELLUM AND BRAIN STEM (ARNOLD-CHIARI DEFORMITY). C. D. ARING, J. Neurol. & Psychiat. **1**:100 (April) 1938.

Aring reports the case of a man aged 20 who showed signs of progressive ataxia with hyperactive tendon reflexes and extensor plantar responses of the lower extremities about twenty-two months before death. In the last four months of life nystagmus, hesitancy in speech and mental changes occurred. There was an excess of protein in the cerebrospinal fluid. Death followed a cerebellar exploration. Pathologic examination revealed a typical Arnold-Chiari deformity, consisting of elongation of the cerebellar tonsils, which were adherent to the medulla by thickened pia-arachnoid; a small, deformed medulla, with degeneration of the rostral half of the olives, and a small pons with degeneration of its transverse fibers. There were also degeneration of the spinocerebellar and pyramidal tracts in the lower levels of the spinal cord and moderate degeneration in the columns of Goll in the upper cervical region. The cerebellum was intact except for the presence of numerous bulbous swellings or "torpedoes" in many of the axons of the Purkinje cells.

MALAMUD, Ann Arbor, Mich.

DISORDERS OF LIPOID METABOLISM AND THEIR RELATION TO OPHTHALMOLOGY. L. VAN BOGAERT, Ann. d'ocul. **174**:410 (June) 1937.

From a comparative study of diseases of lipoid metabolism, such as amaurotic idiocy, Bogaert formulates a new hypothesis. In each condition or symptom a certain lipoid is poorly assimilated; the excesses are stored at first in the reticuloendothelial system, particularly the spleen and liver, then in the lymphatic and the hematopoietic system and, finally, in the bone marrow. When the reticuloendothelial system is incapable of assimilating the lipoid derivatives, the neural and lenticular epiblastic system is impregnated, but because of the vital importance of this system, its involvement is rapidly fatal. According to van Bogaert, "involvement of the reticuloendothelial system constitutes only one phase (initial or intermediary) of a more extensive degenerative process, which finally leads to serious deterioration (circumscribed or generalized) of the vegetative life of the ectodermal cells."

BERENS, New York.

CLINICOPATHOLOGIC STUDY OF AN OLD LESION OF THE RED NUCLEUS. GEORGES GUILLAIN, IVAN BERTRAND and JACQUELINE GUILLAIN, Rev. neurol. **69**:233, 1938.

The authors report the case of a woman who was admitted to the Salpêtrière Hospital at the age of 26 and died there at the age of 71. She had left infantile hemiplegia with choreoathetoid movements, dating at least from the age of 6 years. The limbs of the left side were shortened. The cutaneous plantar reflex on the left was of extensor type. There was left facial paresis, with contracture and spasmodic involuntary movements of the eyelids and peribuccal muscles. The pupils did not react to light. There were interstitial keratitis and iritis bilaterially. The brain presented extensive malacia of the left cerebellar hemisphere in the territory of the posterior inferior cerebellar artery, apparently of relatively recent date. Older malacic lesions destroyed the dorsomedial and central nuclei of the right red nucleus, the lateral radiations of the tegmentum, part of the zona incerta, the pallidotegmental fibers, the nucleus prebigeminalis, the fasciculus retroflexus, the major portion of the dorsal longitudinal bundle, the predorsal bundle and the dorsal decussation of the tegmentum. The dorsomedial nucleus of Edinger was destroyed, but the remainder of the oculomotor nucleus was normal. The entire right side of the midbrain was atrophic. In the pons the left superior cerebellar peduncle was atrophic. The cerebellum showed atrophy of the left hemisphere, almost exclusively cortical. The dentate nucleus showed intense demyelination. In the medulla, the left corpus restiforme was atrophic. The right olivary com-

plex was intensely demyelinated and sclerotic, with marked rarefaction of the ganglion cells. Isolated lesions of the red nucleus are rare. In other cases reported the lesions were more extensive. This case illustrates the connections between the red nucleus, the cerebellum and the olive.

LIBER, New York.

CASE OF MEDULLOBLASTOMA ASSOCIATED WITH THE ADIPOSOGENITAL SYNDROME: CLINICAL NOTE. MARIO FUENTES, Arch. de neurol. y psiquiat. de Mexico **1**:296, 1938.

Fuentes reports the case of a boy aged 11 years who six months after a fall on the head experienced severe headaches, failing vision, vomiting, polyphagia, polydipsia and increase in weight. In the following two years the size of the head increased notably; blindness became complete; headache, vomiting and dizziness continued, and somnolence, disequilibrium and mental retardation, with incoherent speech and a tendency to confabulation, developed. Physical examination revealed a typical adiposogenital syndrome with testicular involution. Neurologic examination showed no definite localizing signs. Lumbar puncture revealed marked increase in pressure. A ventriculogram showed enormous dilatation of the lateral ventricles. Exploration, with a right frontoparietal approach, was performed, but the tumor was not located. Death occurred in a few days. Autopsy revealed a large tumor of the cerebellum, occupying the roof of the fourth ventricle, extending through the aqueduct and spreading to the internal walls of both lateral ventricles, the floor of the third ventricle and the pia over the vermis and cerebellar lobules. The tumor was diagnosed as a medulloblastoma or isomorphous glioblastoma. The author believes that the adiposogenital syndrome was produced by the tumor, although the hypophysis was normal.

MEEHAN, Princeton, N. J.

LOCAL CHANGES IN CONFIGURATION OF THE BRAIN IN CASES OF INCREASED INTRACRANIAL PRESSURE. T. HASENJÄGER and H. SPATZ, Arch. f. Psychiat. **107**:193 (Sept.) 1937.

Hasenjäger and Spatz report the results of their histopathologic studies in cases of increased intracranial pressure, particularly with reference to the phenomenon of inundation of the cistern, described by Spatz, and that of "herniation" of the brain, established by Adolf Meyer. They conclude: 1. In addition to the well known picture of general cerebral swelling, one sees in cases of increased intracranial pressure characteristic changes in configuration of the brain caused by swelling of certain enlarged convolutions, particularly into the basal cisterns. In addition, there may be changes in the basal ganglia, corpus callosum, septum pellucidum and cerebral ventricles produced by displacement of these structures across the midline in cases in which the lesion is unilateral. 2. In cases of bilateral tumors and of swelling of the brain without tumor, when the overflow into the cisterns is symmetric, there is no such displacement. 3. The displacement across the midline and the inundation of the cisterna interhemispherica can be demonstrated in the living patient by ventriculographic and arteriographic examination. 4. These phenomena must be regarded as possible causes of focal symptoms, and care must be taken not to be confused by them in localization of tumors of the brain.

W. MALAMUD, Iowa City.

PONTILE TUMORS. P. BUCY, O. FOERSTER, O. GAGEL and W. MAHONEY, Ztschr. f. d. ges. Neurol. u. Psychiat. **157**:137 (Jan.) 1937.

The authors report a case of intrapontile astrocytoma in which there was a history of twelve years' duration. The case concerned a man aged 35, who showed on examination, palsy of the left side of the face, paralysis of the left abducens nerve, involvement of the eighth, ninth, tenth and eleventh nerves on the left side

and impairment of motor and sensory trigeminal function on the same side. There were partial involvement of the left oculomotor nerve and mild paralysis of the left hypoglossal nerve. There was left cerebellar ataxia. There were no signs of impairment of the pyramidal or sensory tracts. The patient died with signs of bulbar involvement.

Autopsy showed definite enlargement of the left side of the pons and medulla. The left side of the medulla was two or three times as large as the right. Except for the medial lemniscus, none of the long tracts could be demonstrated with the stain for myelin sheaths. Astrocytes were diffusely scattered through the affected parts of the brain stem. Astroblasts and rare spongioblasts were seen. There was rich formation of glia fibers.

The authors comment on the unusually long history. They emphasize the prominence of dizziness, which in this case can be considered as a symptom of focalizing value. There was no contracture of the muscles of mastication, such as has been described in cases of tumor of the pons. The cerebellar signs on the left side were due to involvement of all three cerebellar peduncles on that side. The nucleus of the third nerve was not involved. The partial palsy of the oculomotor nerve was probably due to pressure of the most cephalic part of the tumor on the oculomotor nerve before its exit from the brain stem.

SAVITSKY, New York.

CHANGES IN THE BRAIN IN A CASE OF ADDISON'S DISEASE. E. HAMPEL, Ztschr. f. d. ges. Neurol. u. Psychiat. **158**:91 (May) 1937.

Hampel reports the case of a man aged 23 who had had Addison's disease for eight years. He died in coma. Diffuse glial proliferation was observed in the white substance of the cerebral hemispheres. Demyelination was noted only in the periventricular region. The histopathologic picture suggests that of a toxic process associated with Addison's disease. There was no familial history of diffuse sclerosis.

SAVITSKY, New York.

SUBEPENDYMAL MULTIPLE MALIGNANT GLIOBLASTOMA. F. KENO, Ztschr. f. d. ges. Neurol. u. Psychiat. **160**:297 (Nov.) 1937.

Keno reports the case of a woman aged 52 with an illness of six weeks' duration, characterized by changes in mentality and personality and by terminal hyperpyrexia. The only positive neurologic findings were mild left hemiparesis and a hemianopic field defect. Two large tumors were present in the right thalamus and the right hippocampal region. Both extended to the subependymal region. Multiple subependymal tumor nodules, some of them microscopic, were observed in the walls of the third, lateral and fourth ventricles. The ependymal lining was intact in most places. In a few places tumor cells seemed to break through the ependyma and find their way into the cerebrospinal fluid. Some of these cells were transplanted to distant parts of the ventricle. The transplanted cells seemed to lose some of their malignant properties, for they were usually observed resting on intact ependyma, with signs of degeneration. There was no instance in which metastatic cells were breaking through the ependyma into the subependymal tissue. The aqueductal region was free from tumor foci. The tumor nodules extended as far inferiorly as the calamus scriptorius. The histologic picture was that of malignant spongioblastoma. There was no demonstrable connection between the various tumors. They were probably independent multiple areas of proliferation of tumor cells. The subependymal localization of all the tumors suggests a probable relation between tumor formation and dysplasia.

SAVITSKY, New York.

DEVELOPMENTAL DEFECTS OF THE BRAIN. HANS JACOB, Ztschr. f. d. ges. Neurol. u. Psychiat. **160**:615 (Jan.) 1938.

Jacob describes several types of developmental defects of the brain. The first of these he calls diffuse symmetric delayed migration of ganglion cells. In cases of this anomaly there is a more or less wide band of heterotopic gray matter in the white substance on both sides of the brain, extending almost throughout both hemispheres. The overlying convolutions may or may not be abnormal. In most cases there is a thin layer of white matter separating the heterotopic tissue and the cortex, while in others there is no such line of demarcation. This type of developmental defect is usually associated with microcephaly and pachygyria. Clinically, in these cases there are usually marked mental deficiency and epilepsy. The skull may be microcephalic or normal.

The second type of developmental defect described is called circumscribed delayed migration of gray matter. In such cases there are circumscribed masses of gray matter in the white substance. The overlying cortex is always defective. The surrounding cortex usually shows changes, such as microgyria or polygyria, though it may be normal. A fetal type of porus formation is often observed in association with this type of heterotopia. In some cases the changes are limited to the cerebellum and are often associated with maldevelopment of the spinal cord (gliosis, hydromyelia) and occasionally with internal hydrocephalus and subependymal heterotopias. The skulls may be microcephalic or have normal capacity.

The third type of dysplastic disorder described is that of developmental defect of the cortex. Jacob reports 2 such cases in which the whole cerebral hemisphere and the dorsal part of the cerebellum were involved. Thickened tangential myelinated nerve fibers were seen in the first layer of the cortex; there was poor differentiation of the first and the second layer; small round heterotopic masses in the upper part of the cortex were noted in 2 cases. In 1 case there were myelinated nerve fibers even in the internal granular layer. Ganglion cells were relatively few in areas through which myelinated nerve fibers passed. Similar changes were seen in circumscribed areas in the dorsal part of the cerebellum in both cases and in two from the literature.

SAVITSKY, New York.

GENESIS OF CEREBRAL GLIOMAS. V. G. LAZAREV and A. D. DINABURG, Med. Zhur. **1**:1369, 1938.

Lazarev and Dinaburg, in a study of 80 instances of glioma, found that in 25 per cent an embryonic origin was indicated. From an embryologic point of view, the tumors were divided into four groups: (1) those of dystrophic origin, (2) those exhibiting embryonal foci enabling one to follow the course of development of the growth, (3) those associated with anomalies and developmental malformations and (4) those in which the glioma was associated with gliomatosis. The first group was represented by 7 cases, 6 occurring in children, in which the tumors were localized in the region of the vermis of the cerebellum in the median line, and were designated cytologically as medulloblastomas. The development of these tumors in children, their median localization corresponding to the fissure in the closure of the neural tube—a region giving rise to a number of anomalies and developmental malformations—speaks in favor of an embryonic origin. In 3 of these cases the authors observed hyperplasia of the reticular tissue and felt justified in designating the tumor as a reticuloglioma. In a second group, consisting of 4 cases of astrocytoma, the tumor exhibited a conglomeration of cells identical with "growth centers" described by Obernsdorfer in ganglioneuromas and neurinomas. These growth centers were localized principally in the neighborhood of blood vessels. In some instances they consisted exclusively of elements characteristic of an early embryonic stage (medulloblasts); in others there were seen, in addition, more mature types of cells representing a transition to astrocytes. As a rule, mature astrocytes were seen outside the growth centers. The transitional elements were sometimes observed scat-

tered throughout the tumor tissue. In 1 case of astrocytoma there were observed with the growth centers an additional tumor consisting of embryonal elements. The presence of a second mature astrocytoma in the opposite hemisphere of the brain suggested that growth centers are a manifestation of multicentral growth of the tumor. The third group was represented by 3 cases in which glioma was associated with such abnormalities as heterotopias, irregular formation of the radiations of the cerebellum and development of accessory radiations. The fourth group was represented by 7 cases in which, in addition to the circumscribed growth of the type of astrocytoma, there was observed in the opposite hemisphere gliomatous proliferation representing a developmental anomaly of glial tissue capable of transformation into a genuine glioma under conditions that are still not understood.

EDITOR'S ABSTRACT.

Psychiatry and Psychopathology

METABOLIC, CARDIOVASCULAR AND BIOCHEMICAL CHANGES ASSOCIATED WITH EXPERIMENTALLY INDUCED HYPERTHYROIDISM IN SCHIZOPHRENIA. L. H COHEN and J. H. FIERMAN, Endocrinology **22**:548 (May) 1938.

Cohen and Fierman investigated the physiologic responses of schizophrenic patients to prolonged hyperthyroidization. Eight male schizophrenic patients with advanced deterioration of personality were treated with large oral doses of desiccated thyroid. The basal metabolism rose markedly during two periods of medication, one of rapid, and the other of slow, thyroidization, with a maximum dose of from 15 to 18 grains (0.975 to 1.17 Gm.) a day. It dropped promptly during the period of nonmedication. The weight decreased in all cases. The systolic blood pressure increased under medication and dropped when medication was stopped. The circulatory time decreased with medication, despite considerable random variations, and the pulse rate increased. There was a slight rise in the erythrocyte count, but the leukocyte count was variable. The cholesterol level of the blood showed no change. The total nitrogen level of the blood and urine rose during the medication. The creatinine level of the blood rose during treatment, while the amount of creatinine in the urine showed no changes. The authors think, on the basis of these findings, that schizophrenic patients present factors of resistance, or barriers, to expression of the clinical features of increased oxygen consumption.

PALMER, Philadelphia.

APPROACH TO ASTHMA. JAMES L. HALLIDAY, Brit. J. M. Psychol. **17**:1, 1937.

Halliday reports 30 cases of asthma, with particular emphasis on the emotional factors involved. In each case he endeavors to take into account the person, the environment and the mechanism concerned. He is especially interested in the circumstances under which the first attack occurred, since he finds these are often ignored in a study of asthma. Asthma, he believes, is produced through "the complex triad of the autonomic nervous system, the endocrine glands, and the diencephalon." The diencephalon, where psychologic factors in the environment may "touch" the person, is disregarded by most observers of asthmatic patients. Halliday is impressed with "the prevalence of psychological factors, of emotional reaction, and the emergence of the asthma out of the emotional reaction." He discusses the symbolism of asthma, and thinks that this may be important in determining why asthma appears instead of some other symptom. "Breath" and "life" are closely related concepts in the minds of some persons, and to hold the first may symbolize the struggle to retain the second. The narrowness of the approach is admitted, and Halliday has no desire to "deny the physical." He stresses the point, however, that when psychologic factors

are studied consistently in a series of persons their relevancy to the problem of asthma is high. He maintains that far greater attention should be paid to the psychologic factors in asthma than is usually the case, if the condition is to be understood properly.

ALLEN, Philadelphia.

THE PERFORMANCE TEST BEHAVIOUR OF ADULT MORONS. C. J. C. EARL, Brit. J. M. Psychol. **17**:78, 1937.

Earl believes that tests of performance provide one with a more accurate prognosis than do those of the verbal type, such as the Binet-Simon test, when one is interested in the social adjustability of a young adult moron. "The emotional and temperamental factors which influence their results, and which have earned for tests of the performance type a bad reputation among academic psychologists, actually increase their clinical value. . . . In clinical practice, . . . most defectives have a performance age definitely above the Binet age and unless this is so the prognosis for resocialization is very poor."

ALLEN, Philadelphia.

A NEW OUTLOOK ON THE PHYSIOLOGY AND PATHOLOGY OF MENTAL AND EMOTIONAL STATES. F. A. PICKWORTH, Brit. M. J. **1**:265 (Feb. 5) 1938.

Pickworth suggests that mental disease may be due to disturbance of the blood supply of the brain. At postmortem examination of patients with mental disease yellowish areas can be seen which are in contrast with the normal reddish capillarity of the cortex and basal ganglia. These yellowish areas are due to ischemia. Patchy ischemia permits functioning sections of the cerebral capillary mosaic to become wrongly associated with unrelated sections. Confused behavior results. Mental disorder can therefore be identified with mixing of normal and abnormal capillary mosaic patterns.

ECHOLS, New Orleans.

THE DURATION OF COITUS. G. BOSE, Internat. J. Psycho-Analysis **18**:235 (April-July) 1937.

Psychoanalysis indicates that the male approach to coitus may be determined by two entirely different attitudes: There are men who secure pleasure in intercourse entirely on their own account, without consideration of the partner. On the other hand, there are men whose entire pleasure consists in satisfying the woman; if the woman is unsatisfied the intercourse is considered to be thoroughly unsatisfactory. Women also exhibit similar attitudes. There are women who submit to intercourse for the mere purpose of giving pleasure to the partner; on the other hand, there are women who solicit coitus entirely for their own satisfaction. The duration of coitus is the period of intromission during which erection lasts in the male and during which he is capable of appropriate movement. In a large number of normal men the tendency is to continue the movements from start to finish without break, and the rest periods that are occasionally interposed are, as a rule, dominated by the idea of prolonging the intercourse in order to satisfy the partner. In these persons, the usual duration varies from a minute and a half to five minutes or more. There are also men, apparently normal persons, who can, and often do, continue for from ten minutes to half an hour or more without cessation. In such cases the woman may experience more than one orgasm during intercourse. The woman who experiences repeated orgasm during a single intercourse is not normal. Long duration of intercourse lasting from ten minutes to an hour or more occurs in persons who are obviously abnormal; viz., psychoneurotic, psychotic and castrated persons or those with weak libido. In a certain percentage of these persons there is an absence of orgasm. Erection, which is never strong, gradually subsides,

and coitus ends. Other persons belonging to this class have occasional orgasm. Cases of anesthetic and hysterical women who do not experience orgasm are well known. In coitus the female has, in a sense, an advantage over the male. Her capacity for intercourse does not depend on any physiologic manifestation such as erection. She may choose to play an entirely passive role and may be thoroughly unexcited herself, yet challenge the male to prove his worth when he has no sexual inclination. This method of humiliating the sexual partner is often utilized by the psychoneurotic woman having a conscious or an unconscious antipathy to the husband.

Long duration of coitus is not to be taken as a sign of virility; on the other hand, it is most often an index of repression of feminine cravings on the part of the man. It is the female attitude that prevents the orgastic tendency from coming to a climax. There is often autoerotic repression in such cases, so that real sexual pleasure is wanting. In most cases in which the duration is habitually above eight minutes some disorder exists. The long duration is a sign of weakness of libido rather than of strength.

KASANIN, Chicago.

ANALYSIS TERMINABLE AND INTERMINABLE. SIGMUND FREUD, Internat. J. Psycho-Analysis **18**:373 (Oct.) 1937.

Freud points out that psychoanalytic treatment, which consists in liberating the subject from his neurotic symptoms, requires a long time. Various attempts and technics have been developed to shorten the duration of analysis. Freud has found that the only practical method is to set a date when the analysis is to be finished. He asks what one understands by the ambiguous term "the end of the analysis."

From a practical standpoint it is easily defined. An analysis is ended when analyst and patient cease to meet for the analytic session. This happens when two conditions have been fulfilled. First, the patient must no longer be suffering from his former symptoms and must have overcome his various anxieties and inhibitions, and, second, the analyst must have formed the opinion that so much repressed material has been brought into consciousness and so much inner resistance overcome that no repetition of the patient's specific pathologic processes is to be feared. If, for external reasons, one is prevented from reaching this goal, it is more correct to say that an analysis is incomplete than to say that it has not come to an end.

There is, however, a more ambitious aim, which is to prevent a recurrence of symptoms. Freud points out that the success of therapeutic work depends on the influence of traumatic factors in the production of the neurosis, on the relative strength of the instincts which have to be mastered and on something which is called modification of the ego. The essence of the analytic situation is that the analyst enters into an alliance with the ego of the analysand to subdue certain parts of his id which he has failed to master.

Freud points out that the success of analytic treatment depends largely on the mental health of the analyst himself and his knowledge of his own problems. It cannot be denied that analysts do not in their own personalities come up to the standards of mental health which they demand from their patients. For this, however, the analyst cannot be criticized any more than any internist, who may suffer from the disease for which he is treating his patients. On the other hand, the analyst must be in a position superior to that of the patient if he is to serve as a model for the latter, as frequently he is called on to act as the patient's guide.

Freud points out that analysis is one of the three impossible professions, in which no one can be sure of satisfactory results. The other two professions are bringing up children and the government of nations. Obviously, no one can demand that the prospective analyst should be a perfect human being before he

becomes a practitioner of analysis. The only way in which a psychoanalyst can become qualified is in his own analysis, with which his training begins.

The training in analysis has accomplished its purpose if it imparts to the novice a sincere conviction of the existence of the unconscious, enables him, through the emergence of repressed material in his own mind, to perceive in himself processes which otherwise he would have regarded as incredible and gives him a first sample of the technic which has proved to be the only correct method of conducting analyses. In the practice of psychoanalysis the analyst himself uses many self-defensive mechanisms which enable him to divert the conclusions and requirements of analysis from himself to his patients. The analyst remains as he is and evades the critical and corrective influence of analysis. It is like the old dictum that it is hard for a human being who acquires power not to misuse it. For this reason, Freud stresses that every analyst should submit himself to an analysis at intervals of about five years, without any feeling of shame in so doing. He points out the difficulties of analysis. In women the most severe conflict is envy of the penis, and in men of the struggle against their passive or feminine attitude toward other men. One of the hardest tasks in analysis is to persuade the female patient to abandon the wish for the penis or to convince a male patient that the passive attitude toward another man does not always signify castration, and that in many relations in life it is inevitable. All the analyst can do is to rouse the patient to examine and change his attitude toward things about which he feels most strongly.

KASANIN, Chicago.

RELATION OF INFERIORITY FEELINGS TO GUILT FEELINGS. FRANZ ALEXANDER, Internat. J. Psycho-Analysis **19**:41 (Jan.) 1938.

The psychologic content of conscience consists of a series of primitive emotional sequences. This reaction of conscience can be defined as the expectation of retaliation provoked by one's own hostile aggressions. This expectation is a fearful one; hence it belongs to the category of anxiety and properly can be called fear of conscience. All shadings of the sense of guilt are only quantitatively different: The sense of guilt is always felt as a pressure, as an unpleasant tension—the expectation of an impending evil or of a deserved punishment. If the fear is directed against external persons it is spoken of as fear of retaliation; if it is independent of external objects and is an internal reaction to one's own hostile tendencies it is spoken of as feelings of guilt, or fear of conscience.

As a form of anxiety, the fearful expectation of inevitable and deserved suffering, the sense of guilt is primarily an inhibitory phenomenon. Under its pressure, the subject is likely to avoid the expression of the impulses which have evoked and contributed to his feelings of guilt. At present, there is little doubt that these impulses are exclusively of a hostile destructive nature.

The psychologic content of feelings of guilt may be verbalized as follows: "I am not good. What I want to do (or what I did) is mean or low. I deserve contempt and punishment." In this feeling, in a way, a sense of justice is always implied. One feels guilty because one wants to attack or has attacked some one who does not deserve it.

Feelings of inferiority, on the contrary, have as a rule a stimulating, and not an inhibitory, effect on the expression of hostile aggressions. This explains why feelings of inferiority stimulate competition. One tries to rid oneself of feelings of guilt by renouncing further aggressions or by atoning for them. One tries to free oneself from feelings of inferiority by ambitious competition and by taking revenge on one who has no other fault than being stronger than oneself.

The common neurotic reactions to feelings of inferiority are: (1) increased hostile aggressiveness; (2) an attempt to depreciate the competitor, and (3) fantasy that one is superior, as in megalomania. It is important that in all

these reactions aggressive behavior is stimulated and not inhibited, as in the case of feelings of guilt. In a comparison of the common reactions to feelings of guilt and those to feelings of inferiority it is apparent that the former consists of an inhibition and the latter of heightening of expression of hostile aggressions.

KASANIN, Chicago.

EROS AND APHRODITE. MICHAEL BÁLINT, Internat. J. Psycho-Analysis **19**:199 (April) 1938.

In sexual gratification one must distinguish between "fore pleasure," i. e., sexual play, and "end pleasure," or orgasm. The Greeks had two deities for expressing these two aspects of sexuality—Eros, the mischievous child, representing fore pleasure, and Aphrodite, the mature woman, symbolizing complete genital satisfaction. The mechanism which produces fore pleasure is simple: It generally takes the forms of stroking, tickling, licking or sucking. In adults the corresponding reaction may be smiling, giggling or laughing, or even screaming and crying out. Fore pleasure erotism is for adults a kind of game, something simple, without definite aim, and consequently disjointed and incoherent. The function of end pleasure, on the contrary, is serious and dramatic, if not tragic. It is often even a matter of deadly earnest, for animals of many species die during the first orgasm. Above all, coitus is something definitely in pursuit of an aim: It is not a pastime but a process with a precise intention, a task to be performed. In adults, fore pleasure is related to end pleasure as play is to earnest. It is only when orgasm follows surely on excitation that the youth becomes a man and the girl a woman.

Finally, fore pleasure erotism is manifested by children from the beginning, while there is no doubt that the function of end pleasure is subject to limitations of time. It is not possible to state with any precision when it begins or ends, but the division of human life into childhood, puberty, maturity, the climacteric and old age is based on the phases of the function of end pleasure. The capacity for such pleasure is not originally present, but probably develops during or immediately before puberty and is then slowly and gradually established. In old age it becomes weaker and finally disappears or, at most, makes sporadic appearances. Fore pleasure erotism, on the contrary, is perennial; it begins with birth and ceases only with death.

Fore pleasure is inseparably connected with all somatic functions (e. g., nutrition, digestion, excretion, sense perception and muscular activity). It is probably one of the primal functions of the soma. End pleasure (orgasm) seems to be a relatively recent acquisition. Throughout life there is an alien element in it; it acts on the soma in an intoxicating, or even a stupefying, manner. Also, in contrast to fore pleasure, end pleasure can be dispensed with for some time, and, moreover, the capacity for it does not endure throughout life. It may then be concluded that the soma was originally asexual, incapable of orgasm but not of eroticism, and that at first it knew only fore pleasure, but later, in the course of phylogenetic development, became subject to sexual differentiation and capable of end pleasure.

Fore pleasure is capable of producing, but not of discharging, intense excitation. Any considerable quantity of excitation can be discharged only by means of genital end pleasure. If this outlet is blocked by the resistances due to repression and the only way open to the person is that of fore pleasure, the result is either an anxiety neurosis or some form of morbid craving.

KASANIN, Chicago.

THE SIGNIFICANCE OF THE PREMORBID PERSONALITY IN THE COURSE AND FORM OF PSYCHOSES. E. STENGEL, Arch. f. Psychiat. **106**:509 (June) 1937.

Stengel discusses the influence of the anankastic personality structure in the development of schizophrenic psychoses. He agrees with other authors that the history of a prepsychotic personality of this type does not preclude the development of either a schizophrenic or a manic-depressive type of disease and that usually these constitutional characteristics manifest themselves in the symptoms and course of the disease in a given case. The histories in 4 cases are given.

In 2 cases there was a history of compulsive-obsessive character traits preceding the onset of the psychosis. They expressed themselves in pronounced scrupulousness, pedantry and, later, in fears of being contaminated, with a subsequent compulsion for exaggerated cleanliness and washing. The onset of the psychosis was acute, and the first symptom was coprophagia. The patients stated that they heard voices telling them to perform this act and, in addition, showed delusional and hallucinatory phenomena of other types. The course of the disease was acute and left no doubt of its schizophrenic nature; recovery was followed by return of the obsessive syndrome. The third case was similar except that the obsessive symptoms were characterized by a fear of being seen improperly clothed. The patient heard the voice of the Lord telling her to go out into the street naked. In the fourth case there was, in addition to exaggerated scrupulousness, a pronounced religious trend in the prepsychotic personality, which was followed in the psychosis by denunciation of the existence of God, profane utterings against Him and, finally, development of a set of delusions in which the patient herself became divine, believing herself to be both the wife and the daughter of the Lord. In the last 2 cases the disease was characterized by acute onset, a short course and complete recovery, with return to the previous type of personality, as in the first 2 cases. In none of the cases was there a postpsychotic defect.

The author stresses the fact that the content of the prepsychotic obsessive trends and that of the psychotic delusions and hallucinations seemed to be fundamentally the same, except that the compulsive-obsessive trends were repressed.

The various forms of this type of mental disturbance are divided into three groups. In the first there is a compulsive-obsessive constitutional predisposition which finds its expression in the psychosis. In the second, there is the development of a psychasthenic neurosis, which is followed by a psychosis. Finally, there is the third group in which the obsessive-compulsive phenomena, although related to the special personality structure, must be regarded as part of the psychosis itself. Two points are of practical importance. First, the benign nature and short course of the psychosis are probably due to a strongly developed superego, which throughout the life of the person expresses itself in the psychasthenic symptoms. During the psychosis there is, of course, weakening of the hold of the superego but its influence triumphs over the psychotic disturbance, causing a return to the psychasthenic picture. Second, in treatment of psychasthenia one must carry in mind the possibility that removal of the obsessive symptoms may bring forth the more severe symptoms of a psychosis.

MALAMUD, Iowa City.

PSYCHIATRIC CONSEQUENCES OF OPERATIVE STERILIZATION OF WOMEN. HANS BINDER, Schweiz. Arch. f. Neurol. u. Psychiat. **40**:1 and 249, 1937.

Binder presents a detailed report of the results of examination of 293 women who had been sterilized at least a few years previously. The widely circulated dogma of the harmlessness of operative sterilization is false. Both desirable and undesirable results were encountered in the majority of the author's cases, the disadvantages being considerable in 40 per cent, although in only 10 per cent were they so great as to outweigh the advantages. Aside from its eugenic value in cases of feeblemindedness, certain asocial psychopathic states and many psychoses, sterilization was found to have three principal advantages: protection against aggravation by pregnancy of serious organic disease; alleviation of nervous

exhaustion resulting from repeated pregnancies and the care of an ever increasing number of children, and freedom from anxiety engendered by fear of further pregnancies. Freedom from anxiety was distinctly beneficial in at least three fourths of the cases and led to recovery from definite neuroses in 8 per cent. Sexual relations became more satisfactory as a result of the operation in 30 per cent, and menstruation was favorably influenced in 6 per cent. Sterilization may promote a happier marital existence, improve the general family situation and occasionally bring about disappearance of jealousy on the part of either husband or wife, as well as cessation of infidelity on the husband's part.

Unfavorable results were attributed mainly to an unappeased maternal instinct in 23 per cent of the entire group, sense of a loss of bodily integrity in 14 per cent and feelings of guilt in 3 per cent, making a total of 40 per cent in which the disadvantages were considerable. The sexual life was unfavorably influenced in 20 per cent, and menstrual difficulties were ascribed to the operation in 9 per cent. It was learned that feelings of inferiority resulting from sterilization may lead to paranoid projections or to various forms of overcompensation, such as struggle for power, "masculine protest" and hysterical behavior. No cases of compulsion neurosis were seen, but all other neuroses were found in nearly one-half the cases. A few women became sexually promiscuous after the operation.

Binder mentions the following factors which are likely to influence unfavorably the results of sterilization: the age of the patient, undesirable sequelae being rare in women older than 35 years; a small number of children; a depressive, asthenic psychopathy, more particularly a severe antecedent neurosis; an unhappy marriage; a strongly developed maternal instinct, and religious prejudice against sterilization. The outlook is particularly unfavorable when a woman, suppressing her real desires, seeks sterilization in order to avoid having children by an unloved mate or is forced by her husband to accept the procedure. An unfavorable effect on the sexual life is to be expected in the highly cultivated, maternal and distinctly feminine type of woman, whose weakly developed sexuality has been extensively integrated with the entire personality and is therefore easily disturbed. In conclusion, the view is expressed that, since in a given case desirable and undesirable results both for the individual person and for society may be so inextricably mingled, no hard and fast set of indications for sterilization can be drawn up. The best one can do is to determine from a study of the individual patient whether the possible advantages are likely to outweigh the possible disadvantages.

DANIELS, Denver.

Meninges and Blood Vessels

PURULENT TYPHOID MENINGITIS WITH RECOVERY. P. O. HAGEMAN, Am. J. M. Sc. **195**:497 (April) 1938.

Hageman found that 50 unequivocal cases of purulent typhoid meningitis have been reported in the literature. In all the course was fatal. He reports the case of a man aged 42 who was admitted to the hospital on the twenty-sixth day of the disease because of chills, fever, headache, drowsiness and photophobia. There was intermittent fever for three and one-half weeks after admission to the hospital. Severe headache and increased meningeal irritation usually appeared at intervals of three or four days. Clinical typhoid was not present, or at least was not recognized. The onset was fairly typical of meningitis, and stiffness of the neck was observed as early as the fourth day. The causative organism was a gram-negative rod, isolated from the spinal fluid on four occasions. The characteristic biochemical reactions of Bacterium typhosus were present. The spinal fluid was sterile after the thirty-seventh day of the disease. Clinical improvement was definite; fever persisted, however, through the fiftieth day. The patient was discharged on the sixty-sixth day, apparently in good health.

MICHAELS, Boston.

PAPILLEDEMA ASSOCIATED WITH SUBARACHNOID HEMORRHAGE. J. Q. GRIFFITH JR., W. A. JEFFERS and W. E. FRY, Arch. Int. Med. **61**:880 (June) 1938.

The authors collected from the literature reports on 118 patients suffering from subarachnoid hemorrhage who had undergone satisfactory ophthalmoscopic examination. The occurrence of definite papilledema in a case of proved uncomplicated subarachnoid hemorrhage is unusual. In 78 (66 per cent) the disks were normal, and in 24 (20 per cent) papilledema was present. In the remaining 16 cases (14 per cent) the condition was regarded as equivocal. Experiments were carried out on rats in which colloidal kaolin followed by thorium dioxide was injected into the cisterna magna. Kaolin was found to block the passage of thorium dioxide along the perineural spaces of the optic nerves and to prevent the occurrence of changes in the fundi, even in the presence of a growing tumor of the brain. After experimental subarachnoid hemorrhage, thorium dioxide was likewise blocked from entering the perineural spaces of the optic nerves of 15 of the 20 rats into which it was injected. It was therefore inferred that sufficient blood in the spinal fluid tends to block the perineural spaces of the optic nerves and thus to prevent papilledema.

From a review of the 24 cases of subarachnoid hemorrhage with definite papilledema, the authors found that the papilledema was due to such complicating factors as (1) partial ventricular block, so that relatively little blood reached the subarachnoid space, (2) malignant hypertension, (3) glioma and (4) sinus thrombosis.

BECK, Buffalo.

INVESTIGATIONS ON THE BLOOD-BRAIN BARRIER. U. FRIEDEMANN, J. Immunol. **32**:97, 1937.

Intravenously injected basic dyes, with the exception of satranin, stained brain tissue readily in doses varying from 1 to 7 mg. Of acid dyes, some did not stain the brain at all, while others did, but only in larger doses. The affinity of the dye for brain tissue and the permeability of the cerebral capillaries, which is dependent on the electrical charge of the stain, are determining factors. Staphylococcus toxin, which has a negative charge at the p_H of the blood and the isoelectric point in the neighborhood of p_H 6.2, is unable to pass the blood-brain barrier. It occupies an intermediate position between cobra venom and lamb dysentery toxin, which pass the cerebral capillaries, and botulinus and tetanus toxins. The electrical charge alone proved insufficient to explain the differences in the behavior of the toxins. The differences in the ζ potentials of toxins are, according to Friedemann, better suited to explain the differences in the permeative capacity of the toxins. The ζ potential is the potential difference between the electrical double layer, or the surface of the particles, and the surrounding fluid. It depends on the chemical nature of the colloid and on the p_H of the fluid in which the colloid is dispersed.

DAVIDSOHN, Chicago. [ARCH. PATH.]

DURAL SINUS THROMBOSIS IN EARLY LIFE. O. T. BAILEY and G. M. HASS, Brain **60**:293, 1937.

Frequent recovery from thrombosis of one or both lateral sinuses has long been recognized. Experience with thrombosis of the lateral sinus secondary to mastoiditis has shown clearly that many patients recover, though surgical approach to the sinus is not attempted. Thrombosis of the superior longitudinal sinus is usually considered to be an invariably fatal process in itself or an incident in the terminal stage of various diseases, but Beyers and Hass (1933) showed that the cerebral lesions often are not sufficiently severe to cause death. These authors expressed the belief that some patients with sinus thrombosis and consequent cerebral injury can recover, but they had no definite pathologic proof. In order to determine this, Bailey and Hass made a careful search of the dural sinuses in every patient with a cerebral defect detected at necropsy and observed

organized thrombi in the dural sinuses in 3 instances. Each patient had had normal development up to the time of an acute illness. In 2 instances the illness was accompanied by neurologic symptoms. The illness was followed in each instance by progressive mental deterioration. At necropsy organized and canalized thrombi were observed in the superior longitudinal sinus. Two patients were infants aged 2 and 3 months, respectively, the third a child aged 6 years. In all instances the patients survived the acute attack and lived for several months. The authors believe that these cases support their contention that certain acquired cerebral defects are due to thrombosis of the superior longitudinal sinus and its sequelae. They emphasize the possible relation of cerebral lesions secondary to sinus thrombosis and nontraumatic scars of the cerebrum associated with jacksonian epilepsy. A thorough search of the dural venous sinuses for the presence of organized thrombi may elucidate the etiologic factor in some instances of focal cerebral gliosis, "encephalitis" in childhood and spontaneous subdural or subarachnoid hemorrhage.

SALL, Philadelphia.

ROLE OF THE BOVINE BACILLUS IN ETIOLOGY OF TUBERCULOUS MENINGITIS IN CHILDREN. E. LESNÉ and A. SAENZ, Rev. franç. de pédiat. **13**:457, 1937.

Lesné and Saenz report the results of investigations on tuberculous meningitis in 155 children who had not been subjected to BCG vaccination at birth. It was necessary to eliminate 11 cases in which the culture of the cerebrospinal fluid was sterile and in which the evolution of the disease diverted the diagnosis of tuberculous meningitis to that of curable serous or lymphocytic meningitis. Inoculation of the cerebrospinal fluid into the medium of Loewenstein in the remaining 144 cases always resulted in the culture of tubercle bacilli. In 135 of the cases the bacilli were of the human type, and in 9, of the bovine type. The intravenous injection into rabbits of the strains of bovine bacilli confirmed the cultural diagnosis. All the animals died after from fifty-five to sixty-one days. The authors stress the great sensitivity of the Loewenstein medium and the fact that it permits differentiation of the human and the bovine types of tubercle bacilli before the test on animals is made. The bovine strains that were isolated in the aforementioned cases showed the characteristic properties inherent in this type of bacillus. No atypical or attenuated strains were found. It was found that for guinea pigs the virulence of the bovine strains isolated from the children with tuberculous meningitis was greater than that of the human strains. In discussing the etiologic aspects, the authors stress the following points: The age of the children attacked by the bovine bacillus varied between 18 months and 6 years, whereas the age of the children with the human strains extended to 15 years. Nearly all the children who were infected with the bovine bacillus were either raised or had lived for long periods in rural regions. Indications for familial infection were lacking in the majority of children infected with the bovine strain. Moreover, in all the cases of meningitis due to the bovine bacillus, the source of contamination was raw cow's milk, which had been ingested for long periods. The circumstances were different in the case of the children in whom tuberculous meningitis was caused by the human type of tubercle bacillus. Of these, 92 per cent lived in or near Paris, and only 3.17 per cent lived in rural districts. The majority had been nursed at the breast or were fed with sterilized cow's milk. Human contagion was found in the majority of cases. The authors concluded from these investigations that in France the bovine type of tubercle bacillus plays a much smaller part as an etiologic factor in tuberculous meningitis than is the case in some other European countries, for instance, in England and Denmark, where it is found in from 3 to 42 per cent of cases. Nevertheless, its etiologic importance is not negligable and necessitates prophylactic measures, such as elimination of tuberculosis among cattle, prohibition of the feeding of raw milk to children and strictly controlled pasteurization.

EDITOR'S ABSTRACT.

VELOCITY OF CIRCULATION OF THE BLOOD IN MENTALLY DISEASED PERSONS. D. T. DIMITRIJEVIĆ, Arch. f. Psychiat. **107**:142 (Sept.) 1937.

Dimitrijević reports investigations on the speed of circulation in a series of cases of mental disease. Four groups were studied. It was found that the variations in the speed of circulation were greatest in 10 cases of epilepsy, ranging from six to thirty-five seconds, with an average of sixteen seconds. In 7 cases of dementia paralytica the average speed was nine and nine-tenths seconds, and the variations were negligible. In a group of 30 cases of schizophrenia the speeds ranged from six to thirteen seconds, with an average of eight and three-tenths seconds. Finally, in 5 cases of manic-depressive psychoses there were variations of from six to twelve seconds. The author believes that the differences in the speed of circulation depend probably on peripheral factors in the smaller arteries. Furthermore, there is a definite relation between increase in the speed of circulation and metabolism in general. W. MALAMUD, Iowa City.

INFECTIOUS MONONUCLEOSIS AND MENINGOENCEPHALITIS. V. S. SCHMIDT and A. NYFELDT, Ugesk. f. læger **100**:336 (March 24) 1938.

In the first of the 5 cases of infectious mononucleosis described there were signs of meningitis on admission. Hence, the spinal fluid was examined in the other 4 cases, although no clinical signs of any infection in the central nervous system were seen on admission. In the first 4 cases there were positive agglutination of the blood with sheep blood corpuscles and growth of Listerella in the cerebrospinal fluid. In view of these cases, Schmidt and Nyfeldt suggest that examination of the cerebrospinal fluid is advisable in patients with infectious mononucleosis, especially considering the demonstrated late infection of the central nervous system. Treatment should accordingly be extended beyond the usual clinically demonstrable infectious stage, because of possible sequels in the form of chronic changes due to the involvement of the central nervous system.

EDITOR'S ABSTRACT.

Diseases of the Brain

FUNCTION OF THE MINOR (USUALY RIGHT) CEREBRAL HEMISPHERE IN LANGUAGE. J. M. NIELSEN, Bull. Los Angeles Neurol. Soc. **3**:67 (June) 1938.

Hughlings Jackson postulated that the right half of the cerebrum is capable of serving a language function and that this function concerns largely the automatic use of words. Bianchi in 1906 expressed the belief that the right hemisphere is important in emotional language. Henschen asserted that the right side performs to some extent, although imperfectly, in 60 per cent of cases and that echolalia, paraphasia and senseless reading result from the performance of the right hemisphere. Subsequent work has tended to show that the right side of the brain is capable in many cases of assuming in some degree the functions of the damaged left hemisphere. Nielsen reports briefly 7 cases illustrating the varying degrees to which the minor hemisphere may serve this substitutive function. In 2 intellectually inferior and poorly educated patients, left cerebral lesions were followed by permanent destruction of language function. In the other 5 patients similar lesions were followed by restitution of language function to an extent which varies, at least in part, with the subjects' intellectual ability and education. Nielsen concludes that the minor hemisphere assumes the language function of the damaged left hemisphere in proportion to its ability. MACKAY, Chicago.

INFANTILE CEREBRAL PALSY (SPASTIC PARALYSIS): A DISCUSSION OF THE ETIOLOGY. C. H. HEYMAN, J. A. M. A. **111**:493 (Aug. 6) 1938.

The observations of Heyman are based on a study of approximately 1,000 children with cerebral spastic paralysis. He hopes to amend the prevailing opinion among physicians that spastic paralysis is necessarily caused by obstetric difficulty or trauma at birth. While the importance of birth trauma as an etiologic factor is accepted, it has occupied an unwarranted prominence in the teaching of students and in the minds of the public. Great confusion exists as to what constitutes Little's disease. Strictly, on the basis of Little's description the term should be confined to diplegia associated with difficult or abnormal birth. Actually it is used to include every variety of cerebral palsy present from the time of birth. The term infantile cerebral palsy is preferable to that of Little's disease. Hemiplegia is to be distinguished from paraplegia both clinically and pathologically. Some writers use the term "double hemiplegia," apparently referring to diplegia or quadriplegia. Heyman discusses the causes operating before conception (toxins, infections, neuropathic heredity and consanguinity), during pregnancy (intoxications, primary degeneration, gross developmental defects and syphilis), at the time of delivery (premature birth, difficult delivery at term, asphyxia, anoxemia and air embolism) and during the first few months of life (measles, scarlet fever, pneumonia, whooping cough meningitis or an infectious agent giving rise to some form of encephalitis, probably with minute hemorrhages). Many factors are concerned in giving rise to the clinical picture of the cerebral palsies, and it is impossible to find a cause which applies indiscriminately to all cases. Asymmetric lesions indicate a factor operating before birth.

AUTHOR'S ABSTRACT.

PARIETAL VESTIBULOVISUAL SYNDROME OF TRAUMATIC ORIGIN. G. DE MORSIER, Encéphale **1**:57, 1938.

In 3 cases of trauma to the head well limited lesions were observed in the parietal lobe at operation. All 3 patients had intense paroxysmal vertigo. One patient experienced a sensation of rotation toward the side of the lesion. Another manifestation was clouded vision, giving the impression of a fog or veil before the eyes, which the author calls amblyopia. At times, chiefly during, but also between, attacks of vertigo, there were disturbances in reading with the impression that the letters overlapped. In 1 case amblyopia was associated with hallucinations. At first these were light sensations of elementary colors in which blue predominated. There were blue flames and fields of snow dotted with blue flowers. Later came definite forms, such as swarms of blue butterflies and white pigeons with blue beaks. Finally there appeared micropsic hallucinations—dwarfs 20 cm. tall. At times there were auditory hallucinations. In 1 case the vertigo appeared seventeen months after the trauma. Craniotomy revealed loss of substance of the bone and an epidermal cyst, probably secondary to trauma, which compressed the parietal lobe. In the second case vertigo began twenty days after the accident. Operation revealed a sequestrum of bone at the site of the fracture and a subdural collection of clear fluid. In the third case, in which amblyopia was associated with hallucinations, the trauma was relatively mild and there was no evidence of fracture. There was fluid between the dura and the arachnoid, and the meninges seemed edematous. In all 3 cases marked improvement followed operation. In the first case the symptoms disappeared after the cyst was removed. In this case the lesion, which was well localized, involved cortical areas 5 b and 7 a of Brodmann. It is concluded that this area is the cortical vestibular center. These results are in keeping with the experimental work of Spiegel on dogs and the observation of Foerster and Penfield on electrical stimulation of the cortex in man.

LIBER, New York.

DEMENTIA PARALYTICA BEGINNING WITH APPARENT SYPHILITIC STRIATITIS. HENRI CLAUDE and J. CUEL, Encéphale **1**:97, 1938.

Claude and Cuel report the case of a man aged 37 who began to stammer after experiencing financial and familial difficulties. This was regarded as of psychogenic origin. During conversation the muscles of the face and neck were contracted for several seconds. Except for anxiety and slight impairment of attention and memory, there was no mental disturbance or loss of insight. Psychotherapy was followed by improvement. Later, there was a relapse, this time accompanied by writers' cramp. The cerebrospinal fluid gave strongly positive evidence of syphilis. A diagnosis of syphilitic striatitis was made. Treatment with malaria and bismuth was followed by incomplete regression of symptoms. Finally, seven years after onset of the first symptoms, serious mental deterioration with agitation became apparent. The contractions of the face were still present. There were, in addition, intense dysarthria, tremor and difficulty in walking. The patient died in coma following status epilepticus. Necropsy showed the typical diffuse lesions of dementia paralytica, involving all parts of the cortex and the central gray nuclei bilaterally. The central lesions were no more intense and appeared no older than those of the cortex.

LIBER, New York.

PARASAGITTAL MENINGIOMA OF THE LEFT SIDE, WITH BILATERAL CENTRAL SCOTOMA. M. DAVID, F. THIÉBAUT and M. R. KLEIN, Rev. neurol. **67**:627, 1937.

A man aged 39 for two years had had intense headaches sharply localized in the right frontal region. They were intermittent, but became progressively worse and of longer duration and were often accompanied by vomiting. On one occasion, he lost consciousness and fell. On regaining consciousness he noticed paralysis of the right extremities, which lasted five minutes. Visual acuity diminished progressively. Papilledema was observed bilaterally, but the eyegrounds later became normal. Finally, slight papilledema reappeared and was followed by temporal pallor of the disks bilaterally. Neurologic examination repeatedly failed to show any sign of a focal cerebral lesion. The Wassermann reaction of the blood was negative. The spinal fluid contained 2.8 cells per cubic millimeter and 70 mg. of protein per hundred cubic centimeters. Ventriculographic examination showed that the left frontal horn was pushed down and flattened dorsally. The right frontal horn was dilated, and both ventricles were pushed to the right. At operation a large meningioma was seen to be adherent to the left side of the falx cerebri, without invading it or the sagittal sinus. The tumor had broken into the left frontal horn of the lateral ventricle. A hooklike process extended from the tumor beneath the ventral margin of the falx and depressed the medial surface of the right hemisphere. The mass was removed, in spite of much bleeding. Microscopically, the tumor was a cellular and highly vascular meningioma with a myxoid stroma. The patient made an uneventful recovery. Visual acuity remained low and finally decreased to 1/50 in the right eye and 1/20 in the left, with an absolute central scotoma bilaterally. The right optic disk was completely atrophic; the left, only in the temporal portion.

LIBER, New York.

PSEUDOTUMORAL ENCEPHALITIS WITH ASSOCIATED OCULAR AND AUDITORY DISTURBANCES. G. E. JAYLE, J. E. PAILLAS, A. X. JOUVE and J. BOUDOURESQUE, Rev. d'oto-neuro-opht. **15**:433 (June) 1937.

The basis of this article is the report of the case of a man aged 48 who suffered from violent hemicrania on the right side, accompanied by diplopia, narrowing of the visual fields, especially of the right eye, and lowered vision in the right eye. A similar attack had occurred eighteen months previously. Both attacks were inaugurated by fever. Between the attacks the patient was unable to perform his work as well as theretofore, and there was a constant sensation of heaviness in the head. During the last attack hearing in the right ear was diminished. There

was increasing papillary edema in the right eye and later in the left, without modification of visual acuity. Ventriculographic examination revealed small ventricles and diffusion of the air injected into the subarachnoid spaces. Arterial tension in the retina remained low throughout the course of the illness. Apparent recovery followed the ventriculographic procedure.

The symptoms suggested intracranial hypertension of tumoral origin, but the two febrile periods and the ocular troubles pointed to encephalitis. The papillary edema involved the edge of the disk instead of starting in the temporal sector, as is usual in cases of stasis, and had the appearance of slight congestion with discrete angles in the blood vessels. Visual acuity was 5/10 in the right eye and 15/10 in the left. This lowering of vision was too marked to be caused by beginning stasis and must be attributed to an inflammatory condition. The narrowed visual field also points to an inflammatory process, as does the absence of increased arterial tension in the retina. The more marked narrowing of the visual field for blue than for red and the fact that when papillary edema appeared in the left eye it was not accompanied by lowered visual acuity are in favor of stasis. The conclusion is that both inflammatory and mechanical factors were present. The ventriculographic signs were those observed in the course of encephalic inflammatory conditions and corresponded to the "large brain with small ventricles" described by Vincent.

Reports of similar cases of pseudotumoral encephalitis have been made by Barré and Dereux and Liagre.

Ventriculographic examination is valuable both in diagnosis and in therapeusis. It is interesting to observe the rapidity with which the pathologic signs subside after this operation. The future of patients with subacute or chronic inflammations of the nerve parenchyma is difficult to forecast because of the lack of sufficiently long observation.

DENNIS, San Diego, Calif.

RELATIONS OF THE PREFRONTAL LOBE AND THE VESTIBULAR APPARATUS. A. ROUQUIER and P. LENSEIGNIES, Rev. d'oto-neuro-opht. **15**:439 (June) 1937.

Rouquier and Lenseignies studied 15 patients with unilateral traumatic lesions of the prefrontal lobe. All the patients showed static disturbances of the head and trunk, inclination to the side of the injured frontal lobe, deviation on walking blindfolded, deviation of the extended arms and past pointing to the injured side. None of the patients showed spontaneous nystagmus, hypermetria or dysmetria. In the turning chair test patients with most marked disturbances fell toward the injured side after a few turns to this side as well as to the sound side. Those who did not fall after rotation presented anomalies in deviation of the arms toward the side to which the turning was made. In the case of patients with wounds of the prefrontal lobe the object is to elicit asymmetry, which is probably a functional defect of a highly differentiated regulatory apparatus. This asymmetry is brought out better by the turning chair or the galvanic test. In the latter test, the side toward which deviation occurred and the minimum threshold of intensity needed to produce the deviation were of more importance than the nystagmus. With the positive pole applied to the tragus on the injured side, deviation occurred with one-third the current required for normal persons. In patients in whom the disturbances were accentuated, deviation and rotation of the head always occurred toward the injured side, even when the anode was applied to the sound side. The results confirm those obtained with the turning chair. Deviation of the extended arms was always in the same direction as that of the head. Neoplasms causing bilateral compression of the frontal lobes are accompanied by vestibular hyperexcitability and bilateral inversion of deviation in walking after the turning test.

After lesions of the ascending vestibular pathways Muskens, Leidler and van Gehuchten observed deviation in walking and forced movements of rolling toward the injured side. It is possible that there exists at the level of the

thalamus a relay of the superior vestibular pathways. Studies on degeneration after lesion of the crossing anterofrontal tracts revealed an important ascending pathway uniting the lateral nucleus of the thalamus and the anterior part of the posterior nucleus with the prefrontal cortex. By this pathway, impulses reaching the thalamus from the cerebellum of the opposite side may reach the prefrontal cortex; it is not impossible that impulses from the homolateral labyrinth travel by the same route (Delmas-Marsalet).

Functional disturbance of the frontal lobe causes, first, hyperexcitability of the vestibular apparatus and, next, disequilibrium similar to, but less intense than, that observed after the destruction of one labyrinth. The prefrontal lobe not only is concerned with orientation but is a regulatory center for equilibrium. Its action seems to be bilateral, with homolateral predominance.

DENNIS, San Diego, Calif.

PROBABLE ZOSTERIAN ORIGIN IN A CASE OF SUBACUTE MESENCEPHALOMYELITIS. H. ROGER, Y. POURSINES and J. PAILLAS, Rev. d'oto-neuro-opht. **16**:176 (March) 1938.

This article is the report of the microscopic examination of the neuraxis of a patient whose case has already been reported (*Rev. d'oto-neuro-opht.* **15**:452 [June] 1937). The authors observed dilatation of the vessels, edema of the perivascular sheaths and small hemorrhages in the gray matter under the fourth ventricle. The nuclei of the third, sixth and seventh nerves showed degenerative cellular lesions in the form of lysis of Nissl bodies, ending in the formation of an intraprotoplasmic vesicle, with excentration of the nucleus. Here and there in the white substance of the bulbopontopeduncular region were observed other vascular lesions, characterized by the presence of small, newly formed vessels.

The anatomic study permits the assumption of an infectious etiologic process, probably herpes zoster. At the level of the first cervical segments only did the authors see inflammation of the posterior gray substance characteristic of the zosterian type of myelitis. These lesions consisted of capillary congestion with proliferation of the oligodendroglia and astroglia. The small foci of telangiectatic proliferation in the white columns of the bulbopontile axis may be considered as permanent sequelae of an antecedent zosterian invasion. If zona was indeed the cause, the case demonstrates the polymorphism of motor zosterian disturbances.

DENNIS, San Diego, Calif.

ASYMPTOMATIC NEUROSYPHILIS. J. L. CARRERA, B. REINECKE and M. SEOANE, Prensa méd. argent. **24**:985 (May 12) 1937.

Carrera and his collaborators studied the cerebrospinal fluid of syphilitic patients to ascertain the frequency of asymptomatic neurosyphilis. The group included patients suffering from acquired and congenital syphilis in different stages of the disease, those who had and those who had not received antisyphilitic treatment. Patients showing clear signs of neurosyphilis were excluded. According to the authors, asymptomatic neurosyphilis is rare, especially in patients with congenital syphilis and syphilis of long duration and in patients who have received treatment. In the rare cases in which positive results with tests on the cerebrospinal fluid for syphilis are shown, the common antisyphilitic treatments cause normalization of the fluid, with consequent negative results of the tests. The administration of arsphenamine does not increase the probability of development of asymptomatic neurosyphilis. More intense treatments, such as induction of malaria, are indicated only if the common treatments, given for one or two years, fail to bring the results of the tests of the cerebrospinal fluid from pathologic to normal figures. The only abnormality of the cerebrospinal fluid of 3 patients in

the authors' group was a positive Wassermann reaction. The authors believe that the fact may be due to the presence of reagins in the body humors rather than to involvement of the nervous system by syphilis.

EDITOR'S ABSTRACT. [J. A. M. A.]

STUDY AND TREATMENT OF HEREDOFAMILIAL DISEASES WITH PREDOMINANT LESIONS IN THE SPINAL CORD. R. SOTO ROMAY, Semana méd. **1**:897 (April 28) 1938.

Soto Romay states that the various heredofamilial diseases with predominant lesions in the spinal cord are clinical forms of a process of degeneration of certain segments of the nervous system. The group of familial diseases with lesions in the spinal cord have many common symptoms and analogous anatomicopathologic lesions. The author states that there are atypical types and transitional forms between familial spasmodic paraplegia, progressive amyotrophy of the Charcot-Marie type and Friedreich's hereditary ataxia. In the course of the disease the patient may show transformation of one type to another or the association of two or more atypical forms of the disease. The author reports 3 cases, in a mother and her 2 children. The 3 patients suffered from a combined form of spasmodic paraplegia, progressive amyotrophy and hereditary ataxia. In all 3 cases the factors of heredity and infection existed. Amyotrophy of the distal part of the legs, as well as of the feet and hands, was severe in the mother and in the oldest son, aged 13 years. The disease was of slow evolution in the mother, acute in the son and latent in the daughter, aged 7 years. Microscopic study of the amyotrophic muscle, a specimen of which was taken for biopsy, showed waxy degeneration of the muscular fibers, with loss of striation. There were proliferation of the sarcolemmal nuclei, perivascular infiltration and proliferation of the interstitial tissue. The author reports satisfactory results of combined treatment with vitamins and liver extracts. The evolution of the disease stopped, and the patients gained some muscular force and control of the nervous symptoms. The author calls attention to the diagnostic value and significance of the contralateral Schaeffer sign, which is positive in acute hereditary neurologic diseases and indicates involvement of the pyramidal segment. It was positive in the author's male patient.

EDITOR'S ABSTRACT.

ETIOLOGIC RELATIONSHIP OF TUBERCULOSIS AND MULTIPLE SCLEROSIS. H. AHRINGSMANN, Deutsche Ztschr. f. Nervenh. **143**:133, 1937.

Ahringsmann is interested in the demonstration of a positive complement fixation test for tuberculosis in patients with multiple sclerosis, since he was the first to suggest that multiple sclerosis may be metatuberculosis of the central nervous system. He does not believe that the complement fixation test for tuberculosis (Besredka test) can be compared in specificity with that for syphilis, since it gives from 10 to 20 per cent "false positive" reactions. The question is raised whether the occurrence of a positive complement fixation test for tuberculosis in a patient with a disease of unknown cause is of diagnostic significance. In this regard, it is of value to know that the reaction is positive in from 10 to 20 per cent of nontuberculous persons, in 50 per cent of persons with multiple sclerosis and in 80 per cent of persons with known tuberculosis. On the basis of these statistics, one is not justified in saying that tuberculosis is proved to be a cause of multiple sclerosis, but it can be said that there is a strong probability of such an etiologic relationship. This is the more probable, since no valid objections to this hypothesis have been advanced. The failure of an afflicted person to infect another with multiple sclerosis is not a valid objection when one remembers that tabes dorsalis and dementia paralytica are not thus transmitted.

MERRITT, Boston.

RESULTS OF STUDIES OF CONVULSIONS INDUCED BY METRAZOL. B. WICHMANN, Ztschr. f. d. ges. Neurol. u. Psychiat. **159**:582 (Sept.) 1937.

Wichmann gave metrazol on 183 occasions to 170 patients with various diseases. He used from 3 to 3.5 cc., consuming from fifteen to eighteen seconds for the injection. Epileptic patients were definitely more susceptible to the drug given in this way. Convulsions or their equivalents were noted in 76.76 per cent of the epileptic patients given injections, and in only 7.04 per cent of the other patients. None of the normal subjects used as controls had convulsions. Of the 81 convulsions noted during this investigation, 93.82 per cent occurred in epileptic persons. Patients with symptomatic epilepsy showed an even greater readiness to react to metrazol. The convulsions were like spontaneous seizures. Tremulousness and ticlike movements of the face were often evident. The tonic stage of this induced form of epilepsy lasted from six to sixty-two seconds, and the clonic, from eight to eighty-four seconds. Wichmann suggests the use of metrazol as an additional means of differentiating organic epilepsy and psychogenic convulsions. He emphasizes the importance of giving the injections quickly and in the concentration suggested.

SAVITSKY, New York.

Cerebrospinal Fluid

POLYPEPTIDES OF THE BLOOD AND CEREBROSPINAL FLUID IN DEMENTIA PARALYTICA. H. CLAUDE, J. DUBLINEAU, P. MASQUIN and BONNARD, Encéphale **2**:1, 1937.

Sixteen patients with dementia paralytica were studied before, during and after treatment with malaria or artificial fever. Before treatment the polypeptides of the spinal fluid were increased in 4 of 7 patients to between 22 and 64 mg. per liter, as compared with the normal values of from 5 to 8 mg. per liter. After treatment, the polypeptides of the spinal fluid were diminished in the patients showing favorable results and remained relatively high in those with less favorable reactions. The polypeptides of the spinal fluid were found to be independent of the azotemia, the amount of albumin and globulins in the spinal fluid, leukocytosis, the colloidal benzoin reaction and the polypeptides in the blood.

LIBER, New York.

THE CEREBROSPINAL FLUID IN SYPHILIS. V. KAFKA, Schweiz. Arch. f. Neurol. u. Psychiat. **40**:127, 1937.

Kafka expresses the view that studies of the cerebrospinal fluid in cases of syphilis should include quantitative determinations of the albumin and globulin contents. Estimation of the sugar content may be dispensed with in many cases, but determination of the protein quotient by dividing the concentration of globulin by that of albumin, together with the cell count and the Wassermann and colloidal gold tests, is regarded as necessary. Through examination of many fluids, Kafka and his co-workers have established the lower as well as the upper limit of normal for albumin and globulin and have thus introduced the concept of the "subnormal fluid," a condition in which the fluid has been thinned by influx of water and electrolytes into the ventricles and subarachnoid spaces.

Demonstration of changes in the globulin content which tend to persist throughout the course of syphilis are regarded by Kafka as the most significant result of his studies. Although in fluids in cases of nonsyphilitic conditions globulin must reach a concentration of 20 mg. per hundred cubic centimeters before a normomastic reaction is obtainable, a globulin concentration of 15 mg. per hundred cubic centimeters in latent syphilis, of 12 mg. in tabes dorsalis and of as low as 10 mg. in dementia paralytica will suffice. Conversely, globulin solutions of equal concentration but containing globulin extracted from the spinal fluid in cases of nonsyphilitic conditions, latent syphilis, cerebral syphilis, tabes and dementia para-

lytica, respectively, will give normomastic reactions of increasing intensity, in the order named. These findings, together with differences in the hydration coefficient, indicate that the changes are qualitative as well as quantitative. An increase in albumin without a corresponding change in globulin, occasionally observed in cases of latent syphilis of long duration, is apparently a favorable prognostic sign. In general, however, a high protein quotient resulting from the relatively greater concentration of globulin is characteristic of syphilis, this being true even in cases of congenital syphilis in which the fluid is of low protein content.

In dementia paralytica globulin undergoes a marked increase as compared with the albumin, which is usually decreased, and may even be lacking. Similar, though less pronounced, changes are encountered in tabes, whereas in cerebrospinal syphilis the albumin is not decreased and in the early stages may actually be increased, giving a protein quotient much lower than that in dementia paralytica. A drop in globulin with a corresponding increase in albumin immediately follows malarial treatment of dementia paralytica; these changes become progressively more marked in conditions tending toward remission or recovery, while in those with an unfavorable outcome the globulin-albumin relation characteristic of dementia paralytica is soon regained. The euglobulin content ranges from 4.8 to 48 mg. per hundred cubic centimeters in dementia paralytica, from 2.4 to 4.8 mg. in tabes and from 2.4 to 24 mg. in cerebral syphilis. The decrease of globulin following malarial treatment seems to involve chiefly the euglobulin fraction.

DANIELS, Denver.

INCREASE IN CHOLESTEROL IN THE SPINAL FLUID AFTER ELECTRICAL INJURIES. BERTHOLD WICHMANN, Ztschr. f. d. ges. Neurol. u. Psychiat. **157**:698 (April) 1937.

Holthaus and Wichmann, in 1933, found an increase in cholesterol in the spinal fluid in 3 cases of electrical injury. Since, the cholesterol content of the spinal fluid has been studied a long time after the injury in 16 cases. It was found to be significantly increased in all cases. Fifteen of the patients were unconscious after the injury, 1 for two days. The cholesterol content of the blood was normal. Wichmann believes that this persistent chemical change in the spinal fluid may be due to an injury to the hematoencephalic barrier, with impairment of meningeal permeability.

SAVITSKY, New York.

CHANGES IN THE SPINAL FLUID IN FUNICULAR MYELOPATHY. H. U. GUIZETTI and R. PRÖTT, Ztschr. f. d. ges. Neurol. u. Psychiat. **158**:88 (May) 1937.

Guizetti and Prött studied the changes in the spinal fluid in 80 cases of pernicious anemia in which the average duration of the disease was four years. Severe changes in the spinal cord were shown in 23 per cent. Neurologic examination gave normal results in about 5 per cent of the cases. The spinal fluid was clear except in 1 case. The cell count was normal. In one fifth of the cases the Pandy reaction was mildly positive. The sugar content of the spinal fluid was normal, ranging from 45 to 78 mg. per hundred cubic centimeters. The chloride values were somewhat low, from 68 to 75 mg. per hundred cubic centimeters. The total protein was increased in only 1 case. In 17 per cent, the total protein values were in the upper limits of normal. The globulin was increased in 1 case, and in 8 per cent the globulin-albumin ratio was high. In 17 per cent there were mild changes in the mastic curve toward the left. Changes in the spinal fluid are therefore rare and are not striking. There was no direct relation between the severity of the changes in the spinal cord and the findings in the spinal fluid. There was also no demonstrable correlation between the changes in the blood and those in the spinal fluid. No differences were found in the spinal fluid before and after treatment. The author mentions an unusually refractory case in which the hemoglobin concentration was 14 per cent for six months, and the spinal fluid picture was one of cerebral syphilis, with a characteristic curve but without pleocytosis.

SAVITSKY, New York.

Treatment, Neurosurgery

TREATMENT OF ALCOHOLIC PSYCHOSES WITH THIAMIN CHLORIDE (SYNTHETIC CRYSTALLINE VITAMIN B). M. E. BRODSKY, J. Connecticut M. Soc. **2**:228 (May) 1938.

Up until 1937, when vitamin B_1 extract became available in large quantities, alcoholic psychoses were a serious and unmanageable problem. Since that time it has been possible to treat such conditions with a great deal of success. Of 36 patients whom Brodsky treated, 35 are apparently cured. It is too early as yet to state definitely whether the cure will be permanent. For all the patients with chronic alcoholic psychoses treated the diagnosis was based on a history of alcoholism over a considerable period with hallucinations, particularly of the auditory threatening type, fear and disorientation. The treatment was as follows: (1) the removal of alcohol, if possible, (2) daily injections of massive doses of crystalline vitamin B_1 in the gluteal muscle, the dose being anywhere from 500 to 2,000 units daily and (3) the administration of such a sedative as a bromide, chloral hydrate and, in some cases, phenobarbital. Prompt improvement was observed in all cases within a period of weeks or months and absolute cessation of all symptoms, even though they had lasted for some time. There was no recurrence of a desire for alcohol. This peculiarity was noticed also in patients with acute alcoholic psychoses. These patients were treated with spinal drainage and daily hypodermic injections of vitamin B_1 into the gluteal muscles in small doses, such as from 300 to 500 units; they also showed improvement and lack of desire to return to the former habits. The author is at present conducting a series of experiments to determine whether the human brain contains vitamin B_1 normally and whether it is destroyed by alcohol.

EDITOR'S ABSTRACT.

THE EFFECT OF INDUCED METRAZOL CONVULSIONS ON SCHIZOPHRENIC PATIENTS. HANS H. REESE, A. VANDER VEER and A. H. WEDGE, J. Nerv. & Ment. Dis. **87**:570 (May) 1938.

Reese, Vander Veer and Wedge describe their experiences with metrazol (pentamethylene tetrazol) in the treatment of 41 patients with schizophrenia and compare this method with insulin shock. They had completed the treatment of 20 of the 41 patients. Of these, 4 patients (20 per cent) were discharged with full remissions; 6 (30 per cent) were considered improved, and 10 (50 per cent) were not improved. These figures are much less favorable than those reported by Meduna. Reese, Vander Veer and Wedge compare insulin shock therapy with metrazol treatment, as follows: "With metrazol, if improvement is to occur, it generally appears quickly and proceeds in spurts; with insulin improvement is slow and steady. Insulin cases always exhibit their first lucid intervals in immediate relation to hypoglycemia; metrazol patients do not show improvement until the first or second day after treatment. Stuporous catatonics do not respond well to insulin; in our experience, however, they furnish the most suitable subjects for metrazol therapy. Finally, cases of more than a year's duration show little or no improvement when treated with insulin; the status of such patients when they are given metrazol, however, may change considerably for the better, even though full recovery does not take place." The authors believe that a judicious combination of the two methods seems to promise most. The psychosis in any case must be attacked in time, while the "organized portion of the personality" is resisting the psychotic ideas. Nevertheless, in cases of long standing the patient's condition may be greatly improved.

MACKAY, Chicago.

HYPERTENSION AND ITS SURGICAL TREATMENT. W. M. CRAIG, South. Surgeon **7**:140 (April) 1938.

Craig states that 136 patients with hypertension have been operated on in the section on neurologic surgery at the Mayo Clinic by means of subdiaphragmatic

extensive sympathectomy, without a death at operation and with only 4 subsequent deaths. Clinical improvement after operation varied according to the progress of the disease, the age of the patient and the amount of vascular cardiac and renal damage. Suitable preoperative tests have been devised to measure the amount of potential physiologic response to sympathetic denervation, and these tests have prevented unsuccessful operations and have indicated the cases in which sufficient lowering of the blood pressure or relief from clinical symptoms would take place to make operation justifiable. Operation is advised only for patients whose blood pressure responds satisfactorily before operation to: (1) the slow and intermittent intravenous injection of a 5 per cent solution of pentothal sodium (sodium ethyl l-methylbutylthiobarbiturate) until there is no further drop in the blood pressure, ordinarily, from 500 to 1,000 mg. being injected; (2) the administration of 3 grains (0.2 Gm.) of sodium amytal each hour for three successive hours; (3) the administration of half a grain (0.032 Gm.) of sodium nitrite at intervals of half an hour until six doses have been given, and (4) hourly determinations of blood pressure during rest and sleep for a minimum of twenty-four consecutive hours. If the blood pressure decreases to normal, or nearly normal, as a result of all these measures, the patient may be considered a satisfactory candidate for operation; if not, the effect of operation is almost certain to be unsatisfactory. Operation is contraindicated when the patient is more than 50 years of age and has congestive heart failure, angina pectoris, marked renal insufficiency and/or advanced arteriosclerosis.

EDITOR'S ABSTRACT.

THE VALUE OF CONTINUOUS NARCOSIS IN THE TREATMENT OF MENTAL DISORDER. HARALD A. PALMER, J. Ment. Sc. **83**:636 (Nov.) 1937.

Fifty patients with various types of mental disorders were treated with the diethyldiallylbarbiturate of diethylamine (somnifen). The majority were given a ten day course of treatment. Palmer reports a total recovery rate of 33.3 per cent. The best results were obtained in cases of manic-depressive psychoses, alcoholic psychoses and anxiety states.

KASANIN, Chicago.

THROMBOSIS OF THE POSTERIOR-INFERIOR CEREBELLAR ARTERY (WALLENBERG SYNDROME) TREATED WITH HEPARIN. J. H. MAGNUSSON, Lancet **1**:666 (March 19) 1938.

Magnusson reports beneficial results in the treatment of a woman aged 48 suffering from thrombosis of the posterior inferior cerebellar artery by means of intravenous injections of 150 mg. of a 5 per cent standard solution of heparin. The injections of heparin were given three times a day for five days.

KRINSKY, Boston.

INTRATHECAL SULPHANILAMIDE IN MENINGOCOCCAL MENINGITIS. A. ELDAHL, Lancet **1**:712 (March 26) 1938.

Meningeal infection with organisms alters the rapidity of appearance of the optimum concentration of sulfanilamide in the spinal fluid after oral administration; hence, the intrathecal and intramuscular routes seem advisable. Eldahl treated 12 children, under 4 years of age, with acute meningococcic meningitis by intrathecal administration of from 5 to 30 cc. of an 0.8 per cent solution of sulfanilamide after a slightly greater amount of spinal fluid had been removed. The customary mortality of 70 per cent was lowered to 25 per cent. The patients also received an accompanying dose of from 35 to 150 cc. of sulfanilamide intramuscularly. Spinal drainage was performed daily for the first ten or twenty days of the illness, and later less frequently. Two patients, aged 7 months and 1 year, respectively, had meningococcic septicemia, but recovered. The poor prognosis in cases of this disease is well known.

KRINSKY, Boston.

SERUM THERAPY AND NEW FACTORS IN TREATMENT OF CEREBROSPINAL MENINGITIS. P. ARMAND-DELILLE, C. LESTOCQUOY, J. P. PAILLAS and R. TIFFENEAU, Ann. méd.-chir. **3**:78 (March) 1938.

Treatment of cerebrospinal meningitis by a specific serum has decreased the mortality from 70 to 83 per cent, before 1923, to 15 to 30 per cent. Various factors determine the efficacy of the serum therapy—the age of the patient, the duration of the disease, the organism itself and the type of serum. The authors believe that monovalent serums are more effective than polyvalent serums. They employ intraspinal, intramuscular and subcutaneous methods of administration. They think that repeated spinal drainage is of value. Various drugs have been used in treatment, without much success. Recently, sulfanilamide has been used and has produced the best results in the treatment of meningitis in infants. The daily oral dose is 4 Gm. for adults, 2 Gm. for children and 1 Gm. for infants. The drug can be used subcutaneously in the presence of gastrointestinal disturbances and can also be injected intraspinally, from 5 to 30 cc. of an 0.8 per cent solution being used. As neither serotherapy nor chemotherapy is infallible, it seems advisable to combine the two methods in the treatment of cerebrospinal meningitis.

DE JONG, Ann Arbor, Mich.

TREATMENT OF PURULENT STREPTOCOCCIC MENINGITIS BY SULFANILAMIDE. R. MARTIN and A. DELAUNAY, Ann. méd.-chir. **3**:86 (March) 1938.

Purulent meningitis caused by organisms of the streptococcus group is relatively rare and constitutes only about 6 per cent of the cases of meningitis. In most of the cases the disease is secondary to infectious processes in the ears or nose. The mortality varies from 97 to 100 per cent. Recently, the use of sulfanilamide has been followed by recovery in cases of meningitis of this type. Large doses, up to 0.5 Gm. every two hours, have been given, after which the dose is gradually diminished to 4 and then to 3 Gm. daily. In infants a dose of 0.001 Gm. per kilogram of body weight has been used. In certain cases intraspinal administration is advisable; the authors advocate the use of from 10 to 20 cc. of an 0.8 per cent solution daily, accompanied by drainage of the cerebrospinal fluid. In all cases in which the meningitis is secondary to a localized infectious process, there should also be surgical intervention.

DE JONG, Ann Arbor, Mich.

INSULIN SHOCK THERAPY AT THE PSYCHIATRIC AND NEUROLOGIC CLINIC, BUDAPEST, HUNGARY. B. HORÁNYI-HECHST and A. SZATMÁRI, Monatschr. f. Psychiat. u. Neurol. **98**:101 (March) 1938.

Horányi-Hechst and Szatmári report the results of insulin shock therapy in 64 cases of schizophrenia. In general, the methods of procedure were similar to those recommended by Sakel. Twenty-six patients, or 40.67 per cent, showed complete remissions or remissions with such slight defect that they were able to resume their previous occupational and social activities. In almost half the group the illness was of less than six months' duration, but better results were not obtained with these patients than with the others. Except for mixed forms, the paranoid type of schizophrenia yielded the highest percentage of remissions; of 25 patients belonging to this group, 47.82 per cent exhibited satisfactory remissions. A patient with epileptiform seizures remained unconscious for about thirty hours and died with signs of cardiac collapse. From their observations Horányi-Hechst and Szatmári cannot corroborate the optimistic conclusions of other authors concerning the results of insulin shock therapy. In their opinion the percentage of remissions produced by insulin is not greater than that of spontaneous remissions. Insulin shock therapy may perhaps shorten the duration of the attacks and lead to more satisfactory remissions than those occurring spontaneously, but definite data in proof or disproof of these possibilities are lacking.

ROTHSCHILD, Foxborough, Mass.

JUVENILE DEMENTIA PARALYTICA. JUSTUS STRÖM, Acta psychiat. et neurol. **12**:355, 1937.

Juvenile dementia paralytica is not uncommon; it constitutes 2 per cent of the total number of cases of dementia paralytica. In at least 1 per cent of children with congenital syphilis dementia paralytica develops. Ström reports 4 cases of this condition. In 3 cases the paralytic process began at the age of from 7 to 8 years, and in 1 case, of from 10½ to 11 years. Ström emphasizes the trophic disturbances which he believes have not been sufficiently recognized. These consist in hypoplasia of distal parts of the extremities, with vasomotor disturbances. All the patients were given malaria therapy (from eight to nine paroxysms), followed by a course of bismuth-iodide and arsphenamine. The results were not encouraging. One patient died after treatment. In 2 others an apparent arrest of the disease process was obtained without improvement in the mental condition. Only 1 patient showed sufficient mental improvement for the results to be considered encouraging. The author believes that the only hope of obtaining satisfactory results in the treatment of congenital syphilis lies in prophylactic therapy with malaria before dementia paralytica develops.

YAKOVLEV, Waltham, Mass.

Muscular System

RECURRING MACULO-PAPULAR EXANTHEMS AS PRELUDES TO MARKED EXACERBATIONS IN MYASTHENIA GRAVIS. LEWELLYS F. BARKER, J. Nerv. & Ment. Dis. **87**:416 (April) 1938.

Barker records the case of a Negro girl aged 18 who, after a diffuse rash over the face and arms which lasted two days, noticed difficulty in chewing and in holding the mouth closed. Three weeks later there were ptosis, dysphagia, diplopia and undue fatigue in the arms. In addition to these abnormalities, examination revealed also thickness of speech, nystagmus and weakness of the tongue, the muscles of mastication and the sternocleidomastoid, biceps and abdominal muscles. Injections of prostigmine gave dramatic relief, and the patient gradually improved under medication with ephedrine and aminoacetic acid. After an acute respiratory infection, seven months later, she had a relapse and was again greatly benefited by prostigmine and ephedrine. Eleven months after the second attack a maculopapular rash appeared on the face and arms and spread to the rest of the body. Five days later another exacerbation of the myasthenia occurred, which was alarming in severity. Injections of prostigmine once more gave dramatic improvement, which was maintained by oral administration. Barker leaves the relation of the exanthem to the myasthenia unexplained.

MACKAY, Chicago.

A PRELIMINARY ACCOUNT OF REFERRED PAINS ARISING FROM MUSCLE. J. H. KELLGREN, Brit. M. J. **1**:325 (Feb. 12) 1938.

Pain arising from muscle is always diffuse and is often referred, with the distribution following a spinal segmental pattern. The affected muscles present tender spots on palpation. Kellgren reports 8 cases in which he abolished pain by infiltrating the areas of muscular tenderness with procaine hydrochloride. The pain in some cases may be permanently abolished by this procedure.

ECHOLS, New Orleans.

IS THERE A UNIFORM HEREDITY IN PROGRESSIVE MUSCULAR DYSTROPHY? S. KOSTAKOW and K. BODARWÉ, Deutsches Arch. f. klin. Med. **181**:611 (March 19) 1938.

Kostakow and Bodarwé point out that whereas most investigators agree that progressive muscular dystrophy is hereditary, the mode of transmission is still a

disputed problem. On the basis of a careful study of the literaure and of their own investigations on several groups of families, they conclude that progressive muscular dystrophy is always hereditary. Mutations of the hereditary factors of past generations is the pathogenic basis. The hereditary transmission is not uniform. This lack of uniformity is due to the fact that, in addition to dominant genes recessive genes have a part. There are two genotypically different forms of progressive muscular dystrophy, an infantile and a juvenile type, both of which are hereditary. The authors show six genealogic trees and list the characteristics of the persons indicated in the diagrams. In two of the family groups the hereditary transmission was sex linked and recessive, and in the four other groups the transmission was of the simple recessive type. In one genealogic tree with recessive heredity a marriage between blood relatives was detected in the ascendancy. In this connection, the authors direct attention to the significance of marriages between relatives for the development of progressive muscular dystrophy from a recessive hereditary factor. In the genealogic trees with the sex-linked recessive heredity most of the patients had the infantile type with pseudohypertrophy; in those with the simple recessive heredity there were patients with the infantile and juvenile forms. The causes of death were usually disorders of the respiratory organs; in the patients who survived there was likewise a great susceptibility to diseases of the respiratory organs.

EDITOR'S ABSTRACT.

EXPERIMENTAL STUDIES ON THE ACTION OF PROSTIGMINE IN CASES OF MYASTHENIA GRAVIS. E. KRÜGER and G. SÄKER, Deutsche Ztschr. f. Nervenh. **146**:154, 1938.

Prostigmine prevents the dissociation of acetylcholine in vitro in a manner similar to that of physostigmine. It has been assumed that a disturbance in the function of acetylcholine is the underlying mechanism in the production of myasthenia gravis. The authors consider several hypotheses: 1. The choline reserve of the neuron, from which acetylcholine is made, is diminished and quickly used up. 2. The synthesis of acetylcholine is delayed or diminished. 3. Diffusion of acetylcholine is prohibited by structural changes at the synapse. 4. The amount of esterase is increased, and an originally sufficient amount of acetylcholine is split too quickly to be effective.

The authors' experiments show that prostigmine has a strong inhibitory effect on choline esterase. This effect is less distinct in experiments in vitro, but the difference in the respective effects of physostigmine and prostigmine is shown more distinctly in a comparison of the dissociation of acetylcholine in the blood of normal subjects and of patients suffering from myasthenia gravis before and after injection of these substances. The esterase content was found to be normal in 1 case of myasthenia gravis. The authors conclude that in myasthenia gravis there is a disturbance in a cholinergic mechanism of transmission.

HOEFER, Boston.

SIGNIFICANCE OF CREATINURIA IN PROGRESSIVE MUSCULAR DYSTROPHY. P. NETOLITZKY and E. PICHLER, Wien. Arch. f. inn. Med. **32**:121 (March 31) 1938.

Netolitzky and Pichler demonstrate that in progressive muscular dystrophy the administration of aminoacetic acid causes an increase and later a decrease in the elimination of animoacetic acid without necessarily effecting a clinical improvement. They show further that malaria treatment of progressive muscular dystrophy may be followed by clinical improvement without there being essential changes in the elimination of creatine. Thus improvement in creatine tolerance is no measure of the functional improvement of the dystrophic musculature. Nothing definite is known about the mechanism of creatinuria, but recent inves-

tigations have disclosed that whenever creatinuria is produced experimentally the muscular glycogen is in a state of decomposition. On the other hand, all factors which cause disappearance of the muscular glycogen result in creatinuria. From this the conclusion was drawn that creatinuria is a sign of the disappearance of glycogen from the skeletal musculature. Moreover, it appears that the connection between creatinuria and the disappearance of glycogen applies also to progressive muscular dystrophy and that the resynthesis of creatine and phosphoric acid to phosphagen is impaired. Thus, the conditions may be similar to those which exist in case of poisoning with monoiodoacetic acid. In this type of poisoning the blockage of the carbohydrate metabolism leaves no energy for the resynthesis of phosphagen, and, finally, the stores of phosphagen are entirely depleted. The authors decided to study the fate of the creatine thus liberated, hoping that the results might permit conclusions in relation to progressive muscular dystrophy. In experiments on rabbits they showed that creatine appears only as a result of the intoxication; they think that this suggests that creatine is eliminated because its resynthesis is made impossible by the metabolic disorder elicited by the poisoning. Thus, the creatinuria appears as the result of the impaired relation of free and combined creatine. Whether this mechanism has a part in the creatinuria of progressive muscular dystrophy is still problematic.

EDITOR'S ABSTRACT.

Special Senses

OPTIC ATROPHY IN PERNICIOUS ANEMIA. R. H. KAMPMEIER and EDGAR JONES, Am. J. M. Sc. **195**:633 (May) 1938.

Kampmeier and Jones report 3 cases of atrophy of the optic nerve associated with pernicious anemia. In the first case visual impairment was the presenting and only symptom for six months. Anemia was not sufficiently severe to account for the changes on the basis of ischemia. In the second case the visual disturbance also appeared early; here, too, the anemia could not account for the optic lesion. In these 2 cases the early tentative diagnosis was tabes dorsalis. In 3 of 233 cases of pernicious anemia there was atrophy of the optic nerve. The sudden depletion of blood seemed to be of more importance in the production of the optic atrophy than the degree of anemia. In 2 of the cases the blood counts and hemoglobin values were not low enough to indicate that ischemia was the etiologic factor. The early recognition of visual disturbances in cases of pernicious anemia is essential for the preservation and possible restoration of vision.

MICHAELS, Boston.

CONDITIONED RESPONSES TO LIGHT IN MONKEYS AFTER REMOVAL OF THE OCCIPITAL LOBES. D. G. MARQUIS and E. R. HILGARD, Brain **60**:1, 1937.

Since the experiments of Munk (1890) and Brown and Schäfer (1888), it has been accepted that complete removal of both occipital lobes renders a monkey totally and permanently blind. Subsequent studies have shown that the essential cortical region is coextensive with the anatomic area striata (Poljak, 1932). The question of residual sensitivity to light, however, was raised by Brown and Schäfer. The present investigation by Marquis and Hilgard is based on this problem. The conditioned reflex technic was used. This offers a method by which any residual sensitivity to light can be examined quantitatively. In the present experiments, visual conditioned responses were studied in a series of 5 rhesus and 1 spider monkey before and after bilateral removal of the occipital lobes. In all the animals extirpation of the occipital lobes was observed to have removed the area striata completely. In no instance was any cortex of the striate type seen in sections through the margin of the lesion.

After extirpation of one occipital lobe the monkey showed homonymous hemianopia. After bilateral extirpation of the occipital lobes the animal seemed completely blind. The threat reflex of blinking was permanently abolished, and no evidence of object vision was ever seen in any of the animals. The pupillary light reflex was not significantly affected. The ocular movements were normal.

Conditioned responses to light were established in 3 monkeys after bilateral operations. Except for a slight increase in the latency of response, no difference between the conditioned responses of these animals and those of normal monkeys could be detected. The great similarity of the conditioned responses in the two groups is strong presumptive evidence that the neural mechanism of the response is the same in both cases and that after removal of the occipital lobes the conditioned response is not mediated by a different mechanism functioning vicariously for the visual cortex. More conclusive evidence for this point would be furnished by the demonstration that conditioned responses established prior to operation were retained without further training after bilateral removal of the occipital lobe. This experiment was attempted by the authors in 3 monkeys, with inconsistent results. One monkey retained the response after operation; the other 2 acquired it with retraining.

The results are interpreted as confirmation of the inference that the visual cortex is not the essential neural mechanism for conditioning to light stimuli. The failure of retention in the 2 animals must be ascribed to the effect of shock on other, presumably subcortical, optic centers. Similar abolition of the effects of preoperative training with subsequent relearning has been observed in studies on the effect of removal of the occipital lobes on the brightness discrimination habit in rats (Lashley, 1920) and dogs (Marquis, 1934).

Cerebral localization of the visual functions which remain after removal of the occipital lobes is a problem which cannot be answered finally with the present evidence. There are several reasons for believing that the conditioned responses are mediated by subcortical mechanisms rather than by extraoccipital cortical areas. Anatomic studies (Poljak, 1932) have shown that in the monkey the optic radiation terminates exclusively in the area striata, so that the only pathway of entrance to the cortex for visual impulses must necessarily have been destroyed by removal of the occipital lobes. Furthermore, it has been shown in lower mammals, such as the dog and rabbit, that certain visual functions persist after complete removal of the cortex and must necessarily be subcortical. A critical test of this has not been possible in monkeys because an adequate period of survival after removal of both cerebral hemispheres has not been obtained. Visual function cannot be satisfactorily tested in the hemianopic fields after removal of one hemisphere because of diffusion of the stimulating light to the seeing fields.

SALL, Philadelphia.

MONOCULAR BLINDNESS AS A TRANSITORY REFLEX FOLLOWING ARTIFICIAL PNEUMOTHORAX. BUJADOUX, Ann. d'ocul. **174**:393 (June) 1937.

Bujadoux reports a case of monocular blindness caused by retrobulbar edema, following insufflation of the pleura. Partial recovery of vision followed treatment with acetylcholine, but degeneration of the macular bundle of nerve fibers persisted.

BERENS, New York.

PIGMENTARY DEGENERATION OF THE RETINA AS A DOMINANT HEREDITARY CHARACTERISTIC. J. FRANÇOIS, Ann. d'ocul. **174**:403 (June) 1937.

In a study of 40 members of a family belonging to five generations, François found pigmentary degeneration of the retina in 13 persons (8 males and 5 females). No consanguinity was noted in this series.

BERENS, New York.

ADIE'S SYNDROME IN A CHILD. L. BABONNEIX, H. GRENET and J. SIGWALD, Rev. neurol. **67**:622, 1937.

The authors report the case of a child with paralytic mydriasis and paresis of accommodation of the left pupil. The eyegrounds were of the hypermetropic type. The right eye was normal. The nasopalpebral and cochleopalpebral reflexes were markedly diminished. The achilles and medioplantar reflexes were absent on both sides. The knee jerks, the reflexes of the upper extremities and the various cutaneous reflexes were all normal. All modes of sensation were normal. There was no Romberg sign. The Wassermann reaction of the blood was negative. Examination of the spinal fluid showed no evidence of syphilis. The father was said to have seizures and had been treated with phenobarbital. The mother and 1 sibling seemed to be in good health. The patient was observed for two years; no change in the condition was noted.

LIBER, New York.

ROTATORY LABYRINTHINE TESTS ON PATIENTS WITH CERTAIN LESIONS OF THE TEMPORAL LOBE. G. PORTMANN and P. DELMAS-MARSALET, Rev. d'oto-neuro-opht. **15**:641 (Dec.) 1937.

In 1933 Portmann and Delmas-Marsalet published observations on 2 patients with injuries of the temporal lobe. The only abnormality found in the labyrinthine tests was inverse deviation in walking after rotation. This reaction differs from that found in persons with a lesion of the premotor frontal zone. Two additional cases are reported. The first patient suffered from headaches in the right frontotemporal region, accompanied by occasional attacks of vomiting of the cerebral type. There were also present marked papillary stasis bilaterally, hypertension of the cerebrospinal fluid and slight paralysis of the left facial nerve. A roentgenogram revealed a slight deformity of the right sphenoid bone. There was deviation to the right in walking. The only abnormality discovered with the rotation test (with the head 30 degrees forward) was inversion of the direction of lateropulsion after turning in each direction. Operation revealed a large meningioma in the fissure of Sylvius, which crushed the anterior part of the temporal lobe and compressed slightly the neighboring part of the frontal lobe. The latter lesion probably accounted for the spontaneous deviation in walking. The second patient was operated on for a large abscess of the right temporosphenoid region. Ten months after the operation a typical attack of generalized epilepsy occurred. Neurologic examination revealed nothing abnormal. There was no spontaneous deviation. After rotation in each direction the only abnormality observed was inversion of the direction of induced lateropulsion.

DENNIS, San Diego, Calif.

RELATIONS BETWEEN THE BULBAR CENTERS OF THE VAGUS AND THE VESTIBULAR NERVE. H. PROBY, Rev. d'oto-neuro-opht. **15**:644 (Dec.) 1937.

Proby reports the case of a man aged 43 who in 1915 sustained a fracture of the petrous bone from a bullet wound, resulting in facial paralysis and complete loss of function of the ear. The patient has been under continuous observation for ten years. Suppuration in the ear has been persistent; attacks of vertigo began in 1915 and since 1927 have been accompanied by crises of slowing of the pulse (from 40 to 45 beats per minute), syncope and vomiting. Ocular compression produced slowing of the pulse and sometimes complete cardiac arrest, accompanied by a syncopal sensation. A cardiogram showed no sign of auricular or ventricular contraction during the period of arrest and no disturbance in conductivity of the bundle of His. The seat of the trouble must, then, have been in the extrinsic nerve supply of the heart, the vagus nerve. The left mastoid was exenterated in 1928, and since the cardiac symptoms have clearly improved; there have been no more crises of bradycardia, but the vertigo has persisted in a modified degree. Proby reasons that there is a relation between the cardiac disorder and the labyrinth, the disturbance being due to irritation of the vagus

nerve. Since the peripheral anastomoses of the vagus nerve in the ear are insignificant, the seat of the reflex must be in the region of contiguity in the fourth ventricle of the central nuclei of the eighth and the tenth nerve. The bulbar roots of the fifth nerve and the sensory nuclei of the ninth and tenth nerves are also in close relation with the vestibular nuclei. It is assumed that the degenerated auditory nerve caused changes in the vestibular nuclei, which, in turn, produced irritation and cellular changes, affecting the nucleus of the vagus nerve. There was produced thereby a secondary reflex originating in the nucleus of the vagus nerve and localized in the nerves to the heart. The nucleus of the descending root of the trigeminus nerve is traversed by fibers from the nucleus of the vagus nerve. Thus, the trigeminal nucleus is a mirror, reflecting the condition of the nucleus of the tenth nerve. In this case, the oculocardiac (trigeminosympatheticovagal) reflex has become a reflex with four components, the last being the vestibule. The variable results from ocular compression in cases of labyrinthitis may be explained by the contiguous action of the vagal and vestibular nuclei. The sympathetic and the tenth nerve may exchange not only their fibers but their functions. In animals the sympathetic and the vagus nerve replace each other, if one is absent. It is not surprising, then, that the phenomena of irritation of the two nerves are produced by the same mechanism.

DENNIS, San Diego, Calif.

UNILATERAL PREDOMINANCE OF PROVOKED NYSTAGMUS. G. DE MORSIER and E. BARBEY, Rev. d'oto-neuro-opht. **15**:654 (Dec.) 1937.

Seven patients with unilateral predominance of nystagmus are reported on, 3 of whom had sequelae of concussion, 2 of neuraxitis and 1 each of epilepsy and myasthenia. The phenomenon consists of predominance of nystagmus toward one side after the cold caloric test and reversal of the predominance when warm irrigation is used. The condition, therefore, is not asynergy with lateral predominance of one of the labyrinths but unilateral predominance of the direction of provoked nystagmus, independent of the labyrinth excited. This reaction has been observed in association with a number of lesions of the central nervous system and indicates disturbance of the central vestibular pathways, either from lesions or from vasomotor disturbances. Koch examined 146 patients with craniocerebral traumatism and discovered the reaction in 12, in 7 of whom the reaction appeared only after the hypoexcitability of the labyrinth had disappeared. The unilateral predominance of provoked nystagmus is not always a constant phenomenon. This variability is to be borne in mind in the appraisal of the sequelae of concussion; it indicates a central vasomotor disturbance. An important observation is that the slow component of the predominant nystagmus is toward the same side as the deviation of the body in the Romberg test and is opposite the deviation when the patient walks blindfolded. It indicates a lesion of the central vestibular pathways and not solely one of the brain stem; the lesion may involve the supravestibular pathways, perhaps as far as the hemispheres. Two cases of circumscribed lesions of the frontal and parietal cortex have been observed in which the slow component of the predominant nystagmus was more marked in the direction of deviation in the Romberg test.

DENNIS, San Diego, Calif.

NYSTAGMIC DISSOCIATION. O. METZGER, Rev. d'oto-neuro-opht. **15**:705 (Dec.) 1937.

Metzger defines nystagmic dissociation as "the difference in behavior of the two eyes at the time of nystagmus, whether the latter is spontaneous, revealed or provoked." He and Nordmann described the phenomenon in 1930 in reporting a case of nystagmus retractorius. In that case the eye on the side of the ear being stimulated with cold water revealed horizontal nystagmus, while the opposite eye showed vertical nystagmus, whether the right or the left ear was stimulated. Metzger reports 4 more observations of dissociated nystagmus. These were

made in cases of paralysis of the right internal rectus muscle; tumor of the posterior fossa; encephalitis, localized in the brain stem, and tumor of the left cerebellar fossa. Two mechanisms for the production of dissociation are suggested: (1) the different behavior of the two eyes is explained by unilateral paralysis of one or more ocular muscles, the nystagmus depending on the motor possibilities of the eye; (2) there may be paralysis of associated ocular movements, a central mechanism.

Metzger draws the following conclusions: 1. Nystagmic dissociation is rare. 2. It is always due to disorder of the oculomotor pathways, either peripheral or central. 3. The central type may occur spontaneously, but is brought out better by vestibular stimulation. The importance of crossed immobility of an eye is emphasized. 4. Nystagmic dissociation may reveal a central disorder, which must be situated at the level of decussation of the vestibulo-ocular pathways. 5. Study of provoked nystagmus in different positions of the head will distinguish between peripheral and central dissociation. DENNIS, San Diego, Calif.

PARINAUD'S SYNDROME, WITH PARTICULAR VESTIBULAR AND OCULOMOTOR SYMPTOMS. H. ROGER, M. ARNAUD, G. E. JAYLE and J. E. PAILLAS, Rev. d'oto-neuro-opht. **16**:96 (Feb.) 1938.

The authors report the case of a man aged 32 who for three years had had intermittent diplopia, violent headache, Argyll Robertson's sign and the syndrome of Parinaud. The Wassermann reaction was weakly positive. The ocular symptoms were accompanied by vestibular disturbances. The head was held slightly backward; deorsumvergent, convergent strabismus in the left eye and nystagmus to the left in the right eye were observed. On looking to the right horizontal nystagmus occurred in the left eye, and on looking to the left there appeared horizontal nystagmus in the right eye and oblique, vertical nystagmus, downward to the left, in the left eye. On looking upward the globes did not pass the position assumed when looking forward, and there appeared divergent nystagmus and intermittent nystagmus retractorius. Turning the patient to the right produced nystagmus to the right, persisting longer in the left eye. On turning to the left nystagmus to the right occurred. Douching the right ear with water at a temperature of 27 C. produced no nystagmus, but there were vertigo and deviation of the arm to the right. Douching the left ear produced no effect.

The syndrome of Parinaud is observed in cases of tumor of the pineal region, the quadrigeminal tubercles and the cerebral trunk. Association of spasm of the elevator muscles of the lid with Parinaud's syndrome is not exceptional. In the case reported there was also a spasm of fixation: When the patient fixed on an object the upper lid was retracted more than normal. The asymmetric nystagmus, the sursumvergence or deorsumvergence and the strabismus may be forms of paralysis of function, secondary to peduncular lesions. At operation an inoperable neoplasm of the isthmus was revealed. DENNIS, San Diego, Calif.

Society Transactions

DETROIT SOCIETY OF NEUROLOGY AND PSYCHIATRY

HENRY A. REYE, M.D., *in the Chair*

Regular Meeting, April 21, 1938

A STUDY OF TRAFFIC OFFENDERS IN THE RECORDER'S COURT PSYCHOPATHIC CLINIC. DR. LOWELL S. SELLING.

The apparatus and technical methods used in detection of the personality and physical factors in traffic violations are demonstrated by motion pictures. The following conclusions are reached: In spite of the fact that the traffic division of the Recorder's Court Psychopathic Clinic is only about twenty months old, it has already considered over 500 cases. These cases give one a broad view of what constitutes the personal element in the traffic problem.

The physician has a grave interest in traffic because the proper operation of an automobile requires good sensory perceptions, good coordination and an adequate physical equipment with which to carry out the manipulative requirements. In addition, there is a definite psychiatric problem, since mentally ill, feebleminded and emotionally incapacitated persons are dangerous on the highway because of their bad attitude and poor judgment.

The examination which is made in each case requires four hours and includes: the physical condition, intelligence level and psychophysical mechanisms, as well as attitudes and other psychiatric factors. It has been found that the physical condition is often of importance, particularly in cases of paralysis, one eyedness, lack of a limb or a neurologic disease, such as tabes dorsalis or multiple sclerosis. Vision in relation to the traffic situation is an entirely different factor from that in relation to school achievement and reading ability. Even 20/200 vision may be adequate if a person has good judgment. Color blindness has proved to be of much less importance than is commonly thought, because the nature as well as the position of the traffic lights usually provide facilities for compensating for this defect. In order to make a proper evaluation of whether a person is prone to accident or likely to get into difficulty in traffic it is necessary to test the reaction time and ability to make judgments of depth perception. Generally in persons who are liable to accidents and violations these traits, of themselves, are not of great importance except as indicators of more serious physical handicap.

Most important of all is the psychiatric examination. The person who has an antisocial outlook, even though he may not be strictly "psychopathic," is likely to drive too rapidly and collide with others because he wants the right of way. The inadequate psychopathic person who is compensating for a defect has been found to be worthy of further consideration, but is often responsible for violations and accidents.

The feebleminded, who constitute about 50 per cent of the present clinic population, are highly dangerous; yet a certain number with proper attitudes can operate a car with only small likelihood of getting into difficulty. Senile persons, as they grow older and have both physical and mental deterioration, should be tested and retested because of the possibility that they may deteriorate quickly and become hazardous on the highways. The clinic has seen about 10 psychotic persons, all of whom presented bizarre symptoms which made them a menace to other drivers.

NEW LIGHT ON DELINQUENCY AND ITS TREATMENT. DR. LOUIS ADRIAN SCHWARTZ.

For a better attack on the problem of juvenile delinquency, the forerunner of adult crime, new points of view are obviously needed. Since the results of dealing

with the offender are so frequently disappointing, it must be that the basic forces producing delinquency and the obstacles to treatment have not been sufficiently considered and clarified. Delinquency should be considered as merely one form of human behavior, which is a point of view in marked contradistinction to that of persons who consider merely the negative or destructive aspects of delinquency, who see delinquency merely as wrongdoing, as behavior which is injurious to society, and consequently as concerned with nothing more than utilizing some means to put a stop to this social injury.

The present study, with its long-continued program of treatment for serious offenders, is centered on the family life of delinquents and on a comparison of the delinquent with the nondelinquent child in the same family. The chief value of this research has been the contribution to practical formulation. One of the new orientations resulting from this study concerns itself with the general significance of delinquency as a phenomenon. As a mode of behavior, which is part of the stream of life's activities, it must have as much meaning in the total order of happenings as socially acceptable forms of conduct. It is, therefore, purposive from the standpoint of the individual's needs and urges. Stated in terms of a general principle, the origins of delinquency in every case unquestionably represent the expression of desires and urges which are otherwise unsatisfied. For the offender, like any other kind of conduct, it is a response to inner drives and outer stimuli. From this understanding of the general background of causation, one can discover the nature of the special personal experiences, and the reactions thereto, which have activated the delinquency of the given subject. From this standpoint one can determine for the individual offender the specific meaning of his delinquency. From the experimental studies of treatment a reorientation is obtained with regard to the possibilities of treatment.

The great driving forces which have strong emotional concomitants are the general fundamental desire for ego and affectional satisfactions. Specifically, one must consider the desire for feeling of security in family and other social relationships, for feeling of acceptance by some person or group, for recognition of standing as a personality, for feeling of adequacy, somehow or somewhere. The wish for affectional response is allied to desire for recognition, security and adequacy. Other urges consist of the desire for new experiences and adventures, for outlets for physical and mental energy, for ownership of possessions, for having, seeing and doing. Normally, with increasing age there is also the urge of self assertion, as shown in the desire for emancipation from childhood and family restrictions, for independence and self direction. Interferences with these fundamental wishes are felt by the young person as thwartings and deprivations causing keen dissatisfaction. Some activity must offset dissatisfactions, and delinquency offers one of the possibilities. A striking finding of the research has been the immense amount of discoverable emotional discomfort that clearly has been part of the origins of delinquency. On the other hand, few indeed of the nondelinquent members of the same families had in their emotional lives any such frustrations, and those few had found in channels other than delinquency modes of compensatory satisfaction. The form of the substitutive activity depends partly on external circumstances and partly on consideration of the nondelinquent child, with the thought that it is more astonishing that he has refrained from delinquency than that a brother or sister has shown antisocial behavior. When there have been no intense feelings of deprivations, inadequacies or thwartings as related either to ego impulses or desires for affection, the child has been able readily to find sufficient satisfactions in socially acceptable behavior. Comparative studies of two children in the same family bring this out clearly. This was specially evident in the studies of 8 sets of twins, one of whom was delinquent and one not delinquent. In addition, it was found that great differences were apparent in the feeling of parents and in the latter's behavior toward their different children and that more sympathetic understanding or fulfilment of sentimental needs and less inconsistent treatment had frequently been exhibited from early years toward one

child than toward another. It was clear that in the delinquent group social restraint and inhibitions were in many instances absent because of poor formation of what is so aptly termed an "ego ideal." There had been no strong emotional tie-up to any one who presented a pattern of satisfactory social behavior. It was apparent from the comparative studies that the effectiveness of moral teaching and of good example is dependent on emotional values attached to them by the child. Ethical concepts that have no personification have little force in the lives of young people. In a series of cases in the nondelinquent group, it was apparent that the child sought the esteem of the parent who might even be unworthy, though not considered as such by the child, and that this esteem was obtained and retained if the child remained nondelinquent. . The delinquent child expressed his conscious belief that he was exhibiting wrong conduct, but evidently his feeling about its wrongfulness had not been sufficiently strong to function as a preventive. The introjection of parental prohibitions, the absorption of parental ideas of wrong and right, is the anchorage of conscience long before the principles of good conduct are taught by church or school. Through the earliest prohibitions, even with regard to bodily functions, family possessions or behavior in the family circle, the child develops a conscience long before it comes to any question of social behavior outside the family. The fact seems clear that the barrier which is called "conscience" or the "super ego" is universally found, but in different persons plays various and partial roles in determining or motivating behavior. Hence conscience may cover only certain areas in the field of conduct. In 1 case of our series, a boy evidently had a strong conscience about being mannerly and doing his schoolwork well, while stealing seemed to mean nothing to him except as he might be caught for it. Another important consideration was the origin of the attitudes and beliefs of the parents, because these have much to do with the development of conduct trends in the children. It was often found that certain undesirable attitudes and behavior tendencies exhibited by parents were related to prevalent asocial ideology. Parents who feel deprivations and discomforts, who have not ideals that prevent asocial behavior, can readily rationalize their situation. These ideologies of self-considering individualism militate against the proper upbringing of children and specifically tend to pervade the household, spreading differently from parents to members of the younger generation.

In evaluating the family as a unit, it seemed clear that it was impossible to picture the family life in any single case from statistical statements, even though the series included items of deeper significance than are usually given in social studies. In addition to the more objective considerations of housing, neighborhood conditions and economic status, data on some of the less tangible qualities of family life were included in order to depict the atmosphere and spirit that prevailed in the home. Since many children in these families have avoided delinquency, there must have been possible assets which were hidden in the background of family life. The evil influences of any item could be established only in terms of its meaningfulness for the individual child. One could give many illustrations of surprising and unexpected reactions, such as the concern of a shoplifting mother for the moral welfare of her children and the sympathy of a girl for her immoral mother. Sometimes when either the father or the mother seemed to be an outstanding, unfortunate influence, the other parent appeared to have been much more potent in forming the character of the child. Failure to produce delinquent behavior in a given child depended entirely on the life experience and relationships of that child as contrasted with those of the delinquent brother or sister.

When one compares the dynamic factors in the two groups, the delinquent and the nondelinquent, there is a surprising degree of enlightenment as to the genesis of delinquency. The health history has usually little meaning in a comparison of the delinquent and the nondelinquent group. The obvious exception is found in the case of damage to the brain. A reliable account of severe injury to the head was obtained in 9 instances of delinquency, clearly a much greater proportion than that for the general population.

A careful attempt was made to diagnose delinquency in terms of normality versus personality deviation and normality versus neurosis and psychosis. Patients with diagnoses of neuroses and psychoneuroses exhibited such symptoms as tics and mannerisms, hypochondriacal factors and anxieties, hysterical vomiting, peculiarities in regard to sleep and food, obsessive ideas or compulsive types of behavior. Hyperactivity, aggressiveness and excessive desire for excitement were reported by parents, teachers and others to be habitual characteristics of one third of the total delinquent group. In 25 of 38 cases of physical overactivity, this characteristic had been shown before school age, and in a few it was definite even in infancy. From certain observations it seemed clear that emotional thwarting and dissatisfactions, dating back to very early years, may be the inciting cause of hyperactivity, rather than organic findings. With regard to display of emotions as indicated by moodiness, outbursts of temper and irritability, I can state that about 65 per cent of delinquent persons seemed to show normal emotional balance and control, while about 10 per cent appeared unusually stolid in outward expression of their emotions. From these figures one concludes that such objective signs cannot be relied on to reveal the true facts about feelings that tend reactively to provoke delinquent behavior. Only 25 per cent of the delinquent subjects demonstrated any marked lack of appreciation of the wrongfulness of their conduct, and even then in almost no case was there any attempt at justification of the behavior. Later in life, when criminalistic skills are acquired and material gains result, when current dishonesties are viewed cynically and criminal companionships formed, the story is different.

In about one third of the delinquents, conscious feelings of inferiority were plainly evidenced. About 15 per cent showed, on the whole, marked introverted or extroverted characteristics. One-third were reported to be veritable daydreamers. The startling fact emerged that 75 per cent showed marked dislike of father or mother or of school. Ninety-two per cent were found to be suffering from major emotional disturbances. In 25 cases of delinquency definite diagnosis was made in terms of serious personality deviation, while in only 2 of the cases used as controls was such a diagnosis given. There was a predominance of nervous mannerisms and peculiar physical habits among delinquent children as compared with the subjects in the control group. Mental age levels for the two groups were in only slight contrast. Absences from school in the control groups were due to illness or change of residence, whereas about 60 per cent of the delinquents were truants. Despite the fact that psychologic testing demonstrated superior ability in 14 delinquents as compared with 18 children serving as controls, poor scholarship was registered in 34 per cent of delinquent children as compared with 18 per cent of those in the control group.

In the classification of the total findings relating to the 92 per cent of delinquent persons suffering from major emotional disturbances, the following well recognized diagnostic categories were utilized:

	No. of Cases
Feelings of rejection, deprivation and insecurity, of not being understood, of disturbance in sibling relationships, of being unloved or of withdrawal of love	46
Feelings of being thwarted either in normal impulses or in unusual desires because of earlier overindulgence, or blocking in emancipation of adolescent urges by counteractive pleasure in remaining childishly attached	28
Real or fancied inadequacies or inferiorities in home, school or companionship	46
Intense discomfort about family disharmonies, parental misconduct, parental errors in management or discipline	34
Jealousy toward siblings because of discrimination	31
Confused unhappiness due to deep-seated conflict	17
Need of punishment because of sense of guilt	9

While 14 subjects serving as controls evidently had experienced a considerable degree of emotional discomfort, counterbalancing satisfactions were found in every instance.

In analyzing the material, I may make the following classifications, which parallel the categories of emotional disturbances described:

1. The attempt to avoid, even as a temporary measure, an unpleasant situation by escape or flight from it.

2. The attempt to achieve substitutive compensatory satisfactions through delinquent activities. These satisfactions include the thrill of delinquent adventure, the gratification of obtaining special recognition or attention, perhaps even notoriety, for the offender.

3. In some instances, material gain as compensation for deprivation.

4. The attempt to strengthen and bolster up the ego, which had been lowered by feelings of inadequacy or inferiority, the aim being to obtain recognition and status with the delinquent crowd. This masculine protest was found to be not uncommon among previously effeminate boys.

5. The attempt to gain satisfaction for the ego through direct and conscious expression of revenge attitudes, perhaps through some end design to punish the parents or others by conduct that would make life difficult for them.

6. The attempt to gain a maximum self satisfaction, to inflate the ego, by generally aggressive antisocial attitudes, that is, by exhibition of definite hostilities and antagonisms to authority.

7. The response to instinctual urges felt to be thwarted. While this response might be exhibited in sexual misbehavior, there was discovered notably in delinquents the attempt to satisfy the urge for independence and emancipation, which finally flared up as an adolescent phenomenon.

8. The wish for punishment, especially by others, which was clearly discernible in a few instances. This seeking of punishment through delinquent behavior was always a response to a conscious or an unconscious sense of guilt.

From the studies it readily became apparent that delinquency affords a vehicle for expression of reactions to emotional discomfort. There are many methods of expressing dissatisfaction, and delinquency is one mode.

This new orientation, which seeks to incorporate in as few categories as possible diagnostic criteria extremely significant for determination of plans and possibilities of treatment, leads to three primary groupings.

GROUP 1.—In this group can be classified: (*a*) delinquents who cannot be considered hopeful for treatment, even under ordinarily good conditions of family and community life; (*b*) persons with abnormal or markedly neurotic personality, or those suffering from severe mental conflicts; (*c*) mentally defective persons—any of these who have already shown established delinquent tendencies (weakness of resistance or the special inner stresses of such persons cause them readily to give way to impulses; hence it is unlikely that they will respond to treatment sufficiently to refrain from delinquency).

Future efforts will be possible through prognostic grouping, based on scientifically conducted studies. The protection of society by the establishment of adequate attempts to reform delinquent persons included in group 1 calls for highly specialized treatment, indeed, for experimental reeducational procedures, with provisions for long time segregation and, in some cases, for prolonged psychotherapy while the delinquent is hospitalized, as it were, in a colony or home.

GROUP 2.—In this group should be placed all persons on whom the social abnormality, involving human relationships within or without the family circle, appears to weigh so heavily against possibilities of successful treatment in the home environment that the situation seems largely hopeless. In these cases the facts are so obvious that the prognostic implications should, in all common sense, be clearly recognized in order that there may be economy of effort on the part of those dealing with delinquents, that society may be better protected and that more

reconstructive, and possibly more radical, measures may be carried out. There is required comparatively little investigation, of the type made by the psychiatric social workers in this study, in order to come to a well founded decision about the probabilities of success or failure of treatment in a given situation. Placement in boarding homes results in a remarkably successful adjustment in this group.

GROUP 3.—This group is represented by 67 consecutive cases in which, after thorough investigation and earliest attempts at treatment, the outcome seemed hopeful. The personalities or internal difficulties did not show extreme deviation. The patients came from situations in which the social abnormality did not give evidence of greatly outweighing the chances of successful treatment. This means not that the subjects were less severely delinquent or had not exhibited any signs of abnormality but that the personality difficulty and social abnormality were not so severe or cumulative that they offered insuperable obstacles to therapy. Of the 67 offenders in this group, at the end of the period of treatment 55 had ceased to show delinquency. During a subsequent period of three years, 48 persons (or 72 per cent of group 3) were not delinquent.

Classification of the third group seems to be as clear as that of the others; the prognostic possibilties of treatment are proved by the much greater proportion of successes.

Altogether, it can be seen that this investigation of the fundamental causes of delinquency has left the conviction that the checking of a delinquent career, once started, is not an easy matter. During the last few years, an increasing number of programs have dealt with the mass attack on the problem of delinquency. These projects have taken the form of recreational activities in clubs or settlements, of occupational training in camps, of controls through so-called coordinating councils of any of the various games organized in school systems and similar efforts. It remains to be seen, however, whether persons who have shown serious delinquency can continue to be nondelinquent after such aids to better living are dropped, if such underlying factors as I have discovered in this investigation remain untouched. As a logical result of the study, which shows that the parent-child relationship plays such a huge part in the prevention of delinquent proclivities, I am inclined to believe that the single direct attack of the greatest value may be through widespread parental education—to be sure, not an easy attack. When early signs of delinquency are detected, parents should be educated to act as they should in a case of impending serious illness, namely, voluntarily to seek and carry out the recommendations of professional service in a clinic, to the end that the difficulties may be recognized and expertly treated. Difficulty arises with the attempt of court authorities to force clinical consultations without persuasively educating parents concerning the part they should and could play in uncovering the facts of causation and in remedying them. Research shows definitely that any and all methods of administering treatment for the seriously delinquent will fail unless certain fundamental conceptions that have been outlined as a result of this research are utilized. The practical implications of the study are that little can be accomplished through any organization or system of treatment unless there are recognition of the significance of this new orientation and the development of a personnel to put these principles into practice.

PHILADELPHIA PSYCHIATRIC SOCIETY

BALDWIN L. KEYES, M.D., *President, in the Chair*

Regular Meeting, Oct. 14, 1938

RETROSPECTIVE STUDY OF A CASE IN WHICH HOMICIDE WAS INVOLVED. DRS. THOMAS K. RATHMELL, Norristown, Pa., and KENNETH M. CORRIN.

A psychiatric case is reviewed in which there were personality defects, inspirational fancy and evidence of a paranoid reaction, which was considered rather

typical of dementia praecox, with associated thyroid disease. Homicide brought the patient's psychosis to the attention of the general public.

Necropsy observations, following sudden death while in a state institution, showed massive subarachnoid hemorrhage of the brain in association with hypoplasia of the cerebrovascular system and a ruptured aneurysm (Forbus type) of the circle of Willis.

Consideration is given to the studies of Gellhorn and McFarland which have shown that alteration in cerebral oxygenation may produce disturbances of psychic function in persons otherwise normal and to the circuit of emotion which was proposed by Papez, involving the hippocampus, the anterior thalamic nuclei, the frontal lobe (gyrus cinguli) and the hypothalamus—areas which in this case were inadequately supplied with blood. The question was raised as to the role of the resultant anoxia in the emotional instability noted in the psychosis.

DISCUSSION

DR. D. J. MCCARTHY: This is an extremely important presentation for several reasons. First, in my experience, and it has been one of many years, there is a great deal of carelessness in the physical examination of persons accused of murder.

Usually two or three physicians, who are to examine the accused, go to the prison, where a long conference is held as to the mental status of the accused. The older physician then turns to one of the younger men in the group and says: "Go ahead and make an examination." There is a cursory examination of the reflexes, and the pupils are looked at in a casual way. This is all done from the standpoint of the physical basis of the mental condition. If there is a syphilitic condition, there are serologic tests to guide one. Apart from that, little intensive work is done to determine the physical basis of the mental condition of persons accused of murder.

It would be interesting to find out how much work was done before the experts testified in this case. This case shows the necessity not only for detailed routine examination but for special procedures as well. For instance, the eyegrounds would probably have shown changes in the arterial circulation, suggesting an alteration in the main cerebral blood supply.

From the standpoint of the suggested relation of the aneurysmal condition of the circle of Willis to the mental condition of this patient, it would be well to know more accurately how much arteriosclerosis there was, and, in order to have the whole picture of the cerebral blood supply clearly in mind, the degree of anemia should be determined. In order to work out the factors that form the mental picture when there is disturbance in the cerebral circulation these matters are important.

Not only must these basic factors be considered, but, in addition, all the possibilities of bacteriotoxemia that influence a picture of this kind. Twenty-five or thirty years ago, while working on tuberculosis, I found that it was possible to determine the basis for delusional trends in such factors as these. When the anemia became marked, together with a good deal of mixed toxemia, a mental disturbance began to develop, and as conditions grew worse the mental state changed progressively from normal euphoria to one with delusions of persecution. That I assumed to be due not simply to anoxemia of the cortex but to a complicated condition, including not only the anemia but also the mixed toxemia and all the various factors of faulty function of the other organs of the body resulting from the toxemia. The sum of these factors was the basis for the mental condition.

The delusional trends that developed in those cases could be worked out by means of a psychologic analysis and interpretation, but the reason for the development of mental conditions with delusions of persecution in a certain percentage of patients with advanced tuberculosis lay in the physical factors.

In the case presented here there was only one factor—that of an aneurysm interfering with the cerebral circulation. Whether that would be sufficient to

cause a mental condition is the question. As I understand it, there was in this case another sister or member of the family who had a mental disease. Dr. Corrin, is this true?

DR. K. M. CORRIN: I believe that there was a sister who was accused of shooting a person while she was intoxicated. She was recently held for murder, assault or attempted homicide, but did not have definite mental disease, to my knowledge.

DR. B. L. KEYES: The person mentioned is not a blood relative but a stepsister, whom Dr. McCarthy and I examined recently. She is a chronic alcohol addict and is psychopathic. She has attempted homicide three times while intoxicated.

DR. D. J. MCCARTHY: In this case there is not sufficient explanation in the aneurysm itself for the development of a mental disease unless other factors were associated with it.

It is also, of course, of great interest to students of consciousness to note definite disturbance in the blood supply of certain areas of the brain. Flechsig, thirty or forty years ago, claimed that consciousness can be worked out on an anatomic basis. The term consciousness was used in a broad sense, and I recall that Flechsig, in his discussion, claimed that it was purely relative. A case of idiocy or imbecility he would consider from the point of view of individual consciousness and would maintain that consciousness of that type is not the type of the normal person, but a threshold consciousness. Then, working out the problem of consciousness in the child, he would say: "At what age does this child become conscious?" If one replied: "At the second or third year of age," he would answer that that is not full consciousness; full consciousness develops only when the person appreciates his complete relationship to his social surroundings so to speak. The question of when that period occurs is a relative matter and not anything that can be definitely demonstrated. Is there in this case a study of consciousness in that sense or an alteration of consciousness as the result of periodic disturbances from arteriosclerosis or from the aneurysmal conditions?

As the readers of this paper suggested, their findings throw no new light on the relation of organic factors in the brain to mental disease, but it adds one more item to an accumulation of data of this kind that aids in the study of these cases.

DR. B. L. KEYES: In this case there are two closely allied angles. It is interesting to debate whether this psychosis was due purely to the damage to the circulation of the brain or whether there may have been contributing factors in the environment of the person as she grew up. The stepsister, who purposely shot two people and almost succeeded in shooting a third, did so each time with definite paranoid ideas, which remained even when she was not under the influence of alcohol, though her psychopathic qualities were no doubt influenced by the alcoholism.

The environmental factors, influencing both patients through childhood as they grew up in the same locality, seem to have been much alike. There is nothing to suggest that the circulatory apparatus was in any sense of the same nature, since the patients came from two different families. No neurologic evidence of damage exists in the stepsister thus far. Postmortem observations are not yet possible. She is still incarcerated.

DR. HELENA C. RIGGS: Anomalies of the circle of Willis are not unusual in cases of mental disease. In the series of young patients with such disorders studied by my colleagues and me the average of major anomalies is about 90 per cent. Dr. John Griffiths and I have been interested in the effect of these anomalies on the higher psychic processes. From our own and Hindze's studies we know that anomalies and a high degree of psychic integration are not incompatible. However, since the hydraulic result of the anomalies is to reduce the effective cerebral circulation, we were interested in the relation between psychic disturbances during somatic disease (in which general circulatory efficiency is reduced) and anomalies of the circle of Willis. We studied 373 cases of somatic disease without

associated psychic disturbances and 291 cases in which psychic disorders were exhibited during somatic disease. Anomalies of the circle of Willis were five times as frequent in the cases in which there were psychic disturbances during somatic disease.

THE HISTORY OF CATATONIA—A PSYCHIATRIC CONCEPT. DR. MELVIN W. THORNER.

A consideration of the historical background of the concept of catatonia is presented. This necessarily is concerned largely with the period of greatest development, i. e., the nineteenth century. Commencing with the early schemes of classification of Pinel and Esquirol, the various ideas concerning the syndrome later known as catatonia were developed. The emphasis on single symptoms was shifted to observations of natural disease states with the work of Guislain. Finally, Kahlbaum, in 1874, erected the concept of catatonia in his monograph. While several years elapsed before the concept met with general acceptance, it was finally caught in a new swirl of classification and grouped with dementia praecox by Kraepelin.

DISCUSSION

DR. M. K. MEYERS: It seems that it was Kraepelin who finally grouped catatonia, hebephrenia and other conditions under the term "dementia praecox." I suppose that included most cases of the catatonia of Kahlbaum. I was always under the impression that it was Kraepelin who synthesized the concept of manic-depressive psychoses. I noticed in Dr. Thorner's tables that this had been done before by Baillarger and by Falret. Will Dr. Thorner state whether there was any difference in the conception of manic-depressive psychosis of Baillarger and of Falret and that of Kraepelin?

DR. MELVIN W. THORNER: In his original paper (De la folie à double forme, *Ann. med.-psychol.* **6**:369, 1854) Baillarger described adequately what is now thought of as manic-depressive disease. He mentioned a number of cases in which the various symptom complexes of the manic-depressive state were marked. Some of his descriptions approximate what used to be known as "circular insanity." While Baillarger called the condition in these cases the "psychosis of two forms," I think priority for the description of manic-depressive disease belongs to him.

THE CHRONICALLY AGGRESSIVE CHILD. DR. GERALD H. PEARSON.

Under this caption are included children whose behavior is definitely antisocial and whose attitude toward the family and toward society is overtly hostile. These children show an infantile manner of expressing the aggressive impulse and have not attained sufficient defense mechanisms to socialize it. The average child of from 2 to 4 years shows twenty different defense mechanisms by which he is able to express his aggressive impulses in a socially acceptable manner. Children have difficulty in acquiring such defenses when one or a combination of the following situations are present: (1) a greater than average innate endowment of aggressive instinct; (2) failure of the automatic cortical inhibition of the midbrain centers which govern the liberation of aggressive impulses because of cortical injury or disease; (3) the presence of a need for punishment because of a severe sense of guilt; (4) an aversion toward a strong desire to be a passive dependent person, the aggression here representing a defense against the passivity, and (5) the libidinal rejection of the child, particularly by an overprotective mother.

The chronic aggressive reaction, untreated or treated by the usual psychiatric methods, remains unchecked, is continued as a source of gratification of the need for punishment, is suppressed and changed into sadism or is suppressed by the erection of an obsessional neurosis or paranoid schizophrenia as a defense. Underlying the chronic aggressive reaction are intense anxiety and guilt about loving and being loved. Treatment must attempt to relieve the child of this guilt and anxiety. The chronically aggressive child is hostile to every one; therefore treatment is difficult. Methods of overcoming this hostility to the therapeutist are discussed.

DISCUSSION

DR. K. E. APPEL: In my work, which does not have much to do with such young children, I have been forced more and more to consider these phenomena of aggression, hate and destructiveness that appear in human nature. Yet how many books on aggressiveness and hate are available in psychiatry? Never, psychologically, politically or internationally, was there more need for understanding and discussing the phenomena of aggressiveness and hate than now.

I have wondered why so many books have been written on love and sex and dependency, while the other side of the situation, which is so vitally important, has been neglected. I am not sure that it is not more important to know more about the reactions to frustration and disappointment and the appearance of hate, aggressiveness and destructiveness than about the phenomena of dependency, affection, love and sex. The articles that are available on this topic are not many, and these are difficult to read, even for a person who is familiar with psychoanalytic literature. Dr. Pearson has made an excursion into this field in a way which is understandable and which I think is not available elsewhere.

All these permutations and combinations, these manifestations of impulses that he has mentioned, one may not previously have been aware of. How many have tried to analyze or consider a transference of hate? Most psychiatrists think of transference as a positive matter, as a transference of affection and dependency.

A patient of mine had a depression which seemed to be hopeless. He was sick for eight years, and some of my friends advised me to give up treating him. Increasingly, as time went on, hate and aggressiveness appeared in the patient's relation to me; finally, at the end of about eight years, he became so cross with me that he broke completely and went to Europe. This patient has been well for five years and has had little therapy from psychiatrists since leaving me. I am sure that pushing and working on that patient's destructiveness and hate, which manifested itself primarily with me, was a factor in the cure of the depression. I could cite other cases to that effect, so I think that Dr. Pearson has called attention to an important matter.

Another matter that impressed me in this paper was the relation and relevance of all that Dr. Pearson has said to the treatment of adult psychoneurotic and psychotic patients. As he was discussing this aggressive paranoid reaction to passivity, to inferiority, to a negative masculine complex, I jotted down the names of patients with dementia praecox I have studied recently who seem to have this mechanism so markedly developed.

Dr. Pearson asked what should be done with these patients. One of the patients with whom I have had the best success is a youth aged about 17 who was having great difficulty, had been to all sorts of preparatory schools and had shifted from one to another, staying about six or eight months at one, when he would be put out and go to another. He was not destructive in regard to property. His destructiveness was chiefly verbal, but, except for actual delinquency, it was one of the worst behavior problems that I have met. Thousands of dollars had been spent on him from early childhood, in an attempt to cure colitis. He had had all sorts of injections, rectal and intravenous. I could not see anything in that situation other than that the boy's behavior toward his teachers was displaced aggression toward the physicians who had administered such cruel and painful treatment and toward his parents, who had permitted it. One of the headmasters with whom I talked in conference one day said: "Dr. Appel, the only thing I think should be done to this boy is to thrash him." I said: "I think this is a situation in which I wouldn't do anything to him. I'd not make any rules for him. He needs to work out his resentment against all this cruelty. If he doesn't want to come to school, don't bother about it." I obtained the parent's cooperation. They had tried everything else. I saw the boy twice. The parents and the teachers cooperated, and I had better luck with him than with any other youngster I have ever treated.

DR. F. H. ALLEN: This paper opens a subject that is one of the most important in the understanding of child development, the normal development of a

child's capacity to handle his own aggression and to find in himself a balance between his aggressiveness and his capacity to yield. A child in growing needs an external control to help him experience that aggressiveness toward some one who can both tolerate it and give limits to the way it is translated into overt behavior, so that he can learn the experience of yielding at the same time that he accepts his capacity to assert.

Among the chronically aggressive children that Dr. Pearson has so well described one finds the child who is afraid to yield, who has to be totally assertive. There is the opposite type which Dr. McDonald has described, in which the child has to be as completely nonassertive. The latter type shuts out all aggression by trying to be completely good, while the other exaggerates his aggression to shut out the gentle side of himself. The two sides of the self never get together on any kind of a livable relation with each other.

The normal-growing child achieves this balance between his capacity to be assertive and the need to yield. He finds his relation to those external controls essential for the organization of the emerging self. The overaggressive child is fearful of any yielding and is in constant need of proving his power to remove all limitations. To yield at all means a complete surrender. This more gentle, friendly side of the self has to be shut out by the negative use of aggression.

Dr. J. J. Waygood: I have been interested in the physical background of chronically aggressive children, and it has been my impression over a period of years that the average child of this kind is below normal in size, an undernourished type. All know the reaction to or against inferiority, the overexertion of heart muscle to valvular disease, and are familiar with the overexertion in the field of behavior; it seems to me that this factor plays an important part in the etiology of aggressiveness.

I am sorry that Dr. Pearson cannot be more optimistic about the outcome in the case of these children, but I cannot be any more optimistic than he. The chronic disorder in all lines of medicine is one that yields with great difficulty.

Dr. E. D. Bond: I wish to comment on the case of a girl. She was aggressive, certainly by the age of 6 months, when she bit and scratched her mother's breast, and she continued biting and scratching to the age of 11, when she came to a hospital school for postencephalitic children. What about the part that the institution has to play in the future treatment of such patients? I think my colleagues and I began to do something for her. To do it we had to allow her to run away. She ran away almost every day, took all sorts of chances on the street, picked up men acquaintances, who treated her very nicely, by the way, and, incidentally, during this time ate irregularly and about when and where she pleased. She was losing weight, but gaining in confidence. She began to like the teacher and the physician; she began to catch up in some school activities, which she had never been able to do before. Whether we could have continued that treatment successfully I do not know, but about this time her parents came from New York, saw her, found that she was wandering the streets, that she was getting thinner, abused us with every invective that ever was invented and took her away. They then seized the opposite horn of the dilemma and placed her in a hospital where there was a strict regime, where she was fed by tube, if necessary, at regular times and, of course, was not allowed to run away. In three months she had catatonic dementia praecox.

Dr. J. C. Yaskin: The material presented leads to one thought, that aggression is only a conspicuous feature of a distorted personality. I think I am right in that. The causes enumerated by Dr. Pearson, that is, the feeling of guilt and the passive tendencies, likewise are associated with every, or nearly every, psychopathologic disturbance in the psychoneurotic or constitutionally psychopathic patient. I wondered what Dr. Pearson was going to say about the management of these children. As I see it, he advises institutionalization for the majority of those who cannot be handled at large with ease. Am I correct in that?

Dr. Gerald H. Pearson: Yes.

DR. J. C. YASKIN: It is my impression that aggression is the conspicuous symptom of a great many children who come for psychiatric guidance. What is the fate of the children who do not go to institutions? What happens to the children who are seen by the physician concerned with child guidance? That is a question that I have been asking in this society and elsewhere for a number of years. I know from personal experience that a great many of them become psychotic, go to jail, show the tendencies of the constitutional psychopath or come to the physician later with an obsessive-compulsive psychoneurotic reaction.

But what happens to the children guided carefully in certain places? What are the statistical results for those who have been treated very carefully? I think this is a crucial question, because in a sense it gives an answer as to how worth while child guidance and child psychiatry are. Is it really worth while to expend all the time and effort that have been used? It seems to me that a time has arrived when one should have a numerical answer to this practical question.

DR. GERALD H. PEARSON: Just one point about what Dr. Yaskin said: I believe that the treatment for chronically aggressive children should be an analysis in order to relieve the child of the fear and anxiety which lie behind the aggressive reaction. This is best done in an institution. In the United States so few patients have been treated in this way that no statistics are available as to the ultimate prognosis. The prognosis for patients handled in other ways is poor.

NEW YORK NEUROLOGICAL SOCIETY AND NEW YORK ACADEMY OF MEDICINE, SECTION OF NEUROLOGY AND PSYCHIATRY

CHARLES A. MCKENDREE, M.D., *President of the New York Neurological Society, Presiding*

Joint Meeting, Nov. 8, 1938

BRIEF MANIC-DEPRESSIVE CYCLE AS AN EPILEPTIC PROCESS. DR. RICHARD M. BRICKNER and (by invitation) DR. ALBERT ROSNER.

The goal of the study of intellect and feeling tone is the understanding of these functions in terms of the brain as an organ. The data, so far as human beings are concerned, have been obtained from psychologic studies of normal persons and from patients with varied types of cerebral disturbance. Since the initiation of massive lobectomies by Dandy, a virtually new field has been made available for the study of the subject, especially as it relates to intellect. Investigations on human beings, subsequent to bilateral or unilateral lobectomy, have helped make more concrete knowledge of intellect in terms of brain tissue. By following some of the leads thus obtained, evidence was found concerning the anatomic arrangement of the neurons associated with intellectual function; the aggregate evidence also bore on the question of emotion. It was thought to support the theory that emotion is a derivative function, comprised of the combination of two other functions—feeling tone and thought.

This paper is concerned with the question of feeling tone as a function of neurons. The work of Sherrington, Cannon, Bard and Head and Holmes has indicated that the process of emotion may be considered as a neuronal function, the neurons being located largely in or near the thalamus.

By feeling tone is meant a pure state of feeling unassociated with thought, yet more complex than simple sensations resulting from stimulation of primary sensory pathways. Pure depression and pure elation may be cited as examples. Apparently, studies thus far have rarely dealt with such states in particular. This communication is offered to present evidence that pure depression, and probably

elation, represents neuronal function capable of being elicited by activation of specific neuron groups, much as muscle contraction may be produced by activation of specific neuron groups.

A case is described in which grand and petit mal seizures were exhibited and a briefly sustained feeling of profound depression followed by elation was abruptly precipitated as a minor seizure by the epileptic mechanism. The depression lasted about six seconds, vanishing almost as quickly as it came, instantly to be replaced by an equally vivid feeling of elation, which was similarly short lived. Occasionally the elation was sufficiently intense to result in extravagant manifestations in which the patient, impelled by the wave of feeling, embraced and kissed the nearest person. The depression usually occurred in a strikingly pure form, unadulterated by thought or any other extraneous process. The elation, on the other hand, was less simply constituted because of associated motor components.

That the patient was truly epileptic is indicated by the following facts: (1) The disorder began at an age between 5 and 6 years and has continued to date; (2) the attacks were paroxysmal and characteristically repetitious; (3) the seizures were closely associated with the menses, especially during puberty; (4) periodic generalized convulsions, often nocturnal, sometimes associated with urinary incontinence, were followed by postconvulsive aching of muscles and marked fatigue; (5) electroencephalograms indicated what today are considered characteristic epileptic features.

The Petit Mal Seizures.—Between the age of 5 and 6 years the patient, B., noticed that often during the day she suddenly experienced short episodes of extreme "nervousness," during which for a few seconds the world about her seemed distant and unreal. Gradually, a feeling of melancholy began to replace the nervousness until, after several years, the transient intense melancholy constituted the whole attack. Following these early disturbances the patient recalled distinct, though brief, profound fatigue. It was only later that the melancholy came to be succeeded by elation.

With the onset of menstruation at the age of 13, the transient episodes became progressively more noticeable, not only to herself but to others. Friends informed her that during the attacks she suddenly stopped what she was doing and for a few seconds appeared to stare into space. During puberty the attacks occurred a few days before, during or after the menstrual period, and sporadically at other times. This relationship disappeared in later years. Sometimes seizures were induced or aggravated by excitement or other emotional disturbances; they were not associated with nausea, vomiting, headaches or auditory or ocular symptoms.

B's own account of a typical seizure follows: it occurred while she was under observation in the service of Dr. Henry Riley at the Neurological Institute. The description was dictated by her in response to close questioning.

"I was at Mrs. M's bedside with some of the other girls, and must have been a little nervous and emotional. I could feel myself tense and high strung. There were all those doctors making rounds, and I wanted to know what they were saying. I felt jittery and uneasy, but was able to control myself and acted as usual. I felt it inwardly more than outwardly, though sometimes it takes a great effort to control myself. I didn't suspect I was in for anything and felt pretty well, despite my nervousness. We were all talking about Mrs. D. leaving the hospital.

"As we were talking, for no reason I could understand, I suddenly got that 'very deep feeling,' a gloomy state of mind. The dreariness! I recognized the feeling immediately; it reminded me of other similar attacks, but nothing else was brought to mind—nothing in particular. It's just a state of feeling and not the thoughts that affect me. I didn't think of anything. There was a little quivering in my stomach. I felt removed from the group I was in, and didn't feel one way or another about them or about anything except how I felt. Everything was very impersonal—I didn't lose them, but everything was a little distant; sights and sounds remained."

Concerning her attacks in general, B. said: "During the periods I don't think any faster or any slower. I always go through the same state of mind, with the same pattern. Sometimes the feeling comes so suddenly I can't fight against it, and they pass on soon, but other times they come on less quickly, and I run for a drink of water, and by the time I get to the sink it's all over with. Sometimes I fight against it—I get that blue feeling and try to fight it. I start doing things to work that feeling off me, picking things up, opening my pocketbook, anything. Then, when it overtakes me, it is a little stronger than usual, and I feel all in afterward. The more I fight against it, the worse the attack; the longer I postpone it, the worse it gets me. I come out slower than I go in, and then, pretty quickly the depressed feeling leaves me and everything seems brighter. Then I am so glad. I want some one near me I can love. Everything seems so much dearer to me and I am so happy to be alive. Sometimes, I get very affectionate, I am so happy. I used to take Mr. X. [her employer] and kiss him sometimes, but sometimes I don't end up that way, and they leave me with another depressed feeling, and that usually brings on another, but after that I feel fine again and fear nothing."

The Grand Mal Seizures.—She experienced the first generalized convulsion at the age of 18. Since, she has suffered sporadically from convulsive episodes, occurring at any time during the day or night, all of which were marked by total unconsciousness, frothing at the mouth, postconvulsive fatigue and aching muscles. Occasionally there was loss of sphincter control. The major paroxysms bore no temporal relationship to the minor seizures. The abnormal feeling states as described were limited altogether to the petit mal episodes.

Cases are rare in which the epileptic attack itself, divorced from antecedent or subsequent accessory phenomena, is represented by outbursts of feeling tone. The literature is replete with instances in which the most varied states of thought, feeling or complex automatic behavior precede or follow the attack; Jackson, in particular, devoted his attention to this question.

So-called psychic equivalents are, of course, also well known, in which the seizure is replaced by thought, feeling or behavior of practically any variety. In reports of such cases, the phenomena described, however, are infinitely more complex and less pure than the simple state of feeling exhibited by B.; moreover, because they last longer, they are subject to various additional complicating factors.

Certain approaches to the specific relation between intellect and neural action have been indicated. Can feeling tone be conceived of as a neuronal function? The question is by no means new. However, the opportunity to particularize and crystallize the concept has not arisen often enough to permit thorough exposition; the case of B. is described because the purity and simplicity of her state of feeling seem to offer such an opportunity. Free from any complication, her minor seizures appeared better adapted to demonstration of the main principle of neuronal feeling tone than those in cases in which abnormal states of feeling, usually so complex, preceded, followed or even replaced gross epileptic phenomena. Nonetheless, it is evident that such manifestations illustrate the same principle.

Jacksonian seizures, both motor and sensory, are easily comprehended today in purely spatial terms, the concept of cortical excursion being accepted as a matter of course. Can one, in the same sense, conceive of a jacksonian convulsion of feeling tone in which the elements of explosive onset, intensity of feeling and sudden alteration of mood are similarly visualized in an appropriate neuronal setting? The fact that the epileptic process can at one time ignite a feeling of depression and at another produce a muscle spasm seems to indicate that the former may be as specifically dependent on neural action as the latter.

DISCUSSION

DR. NOLAN D. C. LEWIS (by invitation): I believe that the case which has just been described is one of an epileptic process basically and that the combination of epilepsy and depression in this particular relation is unusual. In support

of the diagnosis of epilepsy there are in the history of the case the facts that the father was egocentric and excitable in temper and that an unusually strong attachment existed between the mother and the child, which has been emphasized by epileptologists time and again. As to the depression, from time to time investigators have concerned themselves with the possible affective components of epilepsy, and attempts have been made to establish some relationship, apparently principally on the basis of the phenomenon of periodicity of attacks existing in both types of disorder. Krisch, in 1928, in a study of 317 cases of manic-depressive psychosis, found that convulsive phenomena were exceedingly rare, that manic attacks and depressive states were also rare in association with epilepsy and that concurrence of epilepsy and manic-depressive psychoses was extremely infrequent. His conclusions probably expressed the current opinion when he decided that a relation between the two diseases is unlikely.

Moreover, one finds that suicide and self mutilation are exceedingly rare in cases of epileptic disorders, for reasons that I shall not take time to discuss. As far as depression is concerned, one finds it in practically every variety of mental disease. For instance, practically all schizophrenic states start with depression, which may or may not be endogenic. It may be in keeping with the life situation of the patient and incidental to his failures and difficulties in adjustment. The German psychiatrist Neumann, many years ago, stated that in his opinion there is only one mental disease and that the disorder has four symptoms; viz., excitement, elation, depression and confusion. On this basis, classifications of mental disorder are made by arranging combinations and entities of these four symptoms. This statement is made merely to emphasize that depression is common in a wide variety of mental disorders; of course, it appears from time to time in the life of the epileptic patient, but I doubt whether a depression appearing in this situation is of the pure endogenic variety. I suspect that it is usually, if not always, incidental or reactive in type.

Permit me to quote one sentence from the authors' paper: "The fact that the epileptic process can . . . ignite a feeling of depression and at another produce a muscle spasm [shows] the former may be as specifically dependent on neural action as the latter." I believe that most psychiatrists would not take exception to this hypothesis, but there is some question as to whether the case as presented proves the hypothesis. Is this case one of depression in the ordinary sense in which the term is used? I have the impression that states of depression in the epileptic situation differ from other states of depression. I believe that these short shifts in reaction, which look like affect, are chiefly transitory states of confusion. These states may be transitory disturbances of consciousness of some degree, with motor manifestations and sense deception. Slight obscurations of consciousness in the epileptic person are not infrequently accompanied by short hypomanic-like activity or, on the other hand, by heaviness and inactivity. Is the patient merely using words such as "sadness" and "depression" to indicate a feeling of heaviness or to express a disagreeable feeling for which she has no adequate vocabulary? The patient herself has said that she has no thought component in connection with this feeling. It is my impression that the patient probably had a feeling of heaviness or a sense of confusion or inertia for a very short period and that this was not a true depression, on the one hand, or a true hypomanic expression, as described for her more active affective-like states, on the other. Disturbances of consciousness with affective-like components are, of course, extremely common in association with epilepsy.

DR. HANS STRAUSS: The case reported demonstrates clearly that the emotional syndromes of depression and elation can appear as the manifestation of an epileptic process. The authors have used this observation to show that these emotional states can be produced by the activation of specific neurons. This conclusion may also be reached from observations made in cases of coarse organic lesions of the brain. I shall always remember a patient whom I observed in 1925 in Professor Foerster's service at Breslau, Germany. The patient had a craniopharyngioma which had grown upward into the third ventricle and into the head of the left

caudate nucleus. She showed a pronounced manic state without amnesic symptoms. She was always in good humor, joked continuously and was very talkative. During the operation a cyst, forming a part of the tumor, was punctured and emptied. After this procedure the manic syndrome disappeared immediately. This case was reported nine years later by Foerster and Gagel (Ein Fall von Ependymcyste des III. Ventrikels, *Ztschr. f. d. ges. Neurol. u. Psychiat.* **149**:312-344, 1934). In the same paper additional cases were reported, one of which I think is worth mentioning here. In this case operation was performed for a papilloma of the plexus of the third ventricle. During the operation there occurred a hemorrhage in the third ventricle. When the surgeon, in sponging the blood, touched the floor of the third ventricle close to the infundibulum the mental state of the patient, which had been normal so far, changed immediately and completely. There appeared a manic syndrome: the patient laughed, whistled, talked a great deal, made obscene remarks, proposed to the woman assistant controlling the pulse and patted her hand. As soon as the surgeon ceased to touch the infundibular region this syndrome disappeared, but it reappeared as often as this region was touched and never when any other area was touched.

This shows that the manic syndrome can be provoked by interfering with the activity of specific neurons. These, it seems, are situated in the floor of the third ventricle, close to the infundibulum. I wonder if future observations will show that epileptic attacks of the type described by Dr. Brickner and Dr. Rosner are characteristic of the infundibular region and whether their presence will help to localize lesions in this region.

DR. FRANK FREMONT-SMITH: Several years ago I studied a number of patients with typical epileptic convulsions some of whose attacks, as in this case, were precipitated by emotional factors. In a few instances the petit mal attacks were not dissimilar from those in the case reported tonight in that they were associated with a feeling of sadness, or more commonly with a feeling of fear. No conscious thought processes accompanied this feeling. It appeared to be pure affect. Nevertheless, by further questioning, particularly by asking whether this feeling of sadness brought to mind any previous situation in their lives associated with a similar feeling, the patients in several instances remembered a long-forgotten episode which had been accompanied by the same emotional tone which they now felt during the petit mal attacks. Moreover, in some instances it became evident that the petit mal attack was precipitated by a stimulus which, although apparently innocuous, actually was directly related to the forgotten episode. It is also fair to say that many so-called normal persons have short, transitory periods of depression or of mild elation for which it is difficult to find a cause. At times, however, the occasion for the feeling tone is suddenly remembered. It is difficult, therefore, to be sure that what appears to be pure affect may not have an intellectual aspect which has been repressed, with a forgotten episode. If this were so, however, it would not in any way be opposed to the concept that affect is associated with neural discharge.

DR. JOSHUA ROSETT: Feelings of elation or depression as a premonitory symptom of an epileptic seizure are not uncommon. The conclusion that since feelings of elation and depression were followed in this case by muscular activity, feeling in general must be the result of neuronal activity is difficult to understand. I do not doubt in the least that feeling is the result of nerve activity, but how is this proved by the case in question?

DR. LUIS R. PERELMAN (by invitation): A patient with true epilepsy who attended the clinic could almost induce a grand mal attack by listening to sad music on the radio.

DR. RICHARD BRICKNER: I cannot agree completely with what has been said in the discussion. I must differ with Dr. Lewis in one respect—namely, that when the patient said she felt sad one can interpret it as meaning that she was confused; one did not know how she felt. One must believe patients when they say they feel a certain way and, unless there is a good reason, I think one should

not deny their statements. Moreover, that this patient was not confused is indicated in several ways. During the attacks she was able, deliberately, to bring on thoughts and tried to do various things to shake off the feeling of depression. She would try to say something or would open her bag and close it, all with the deliberate intention of making the feeling cease. That seems to show that she did know what she was doing. Also, there were other times when an attack was not as clearcut as those described, when it was not simply pure depression. Sometimes thoughts were linked with it; when that was so she knew what they were and could repeat them afterward. All these things indicate that she was anything but confused.

Dr. Rosner and I are grateful to Dr. Strauss for having referred us only last week to the cases of Dr. Foerster. They are excellent, and it seems to me that they fit in perfectly with our purpose, to show that a pure state of depression (and perhaps elation) can be specifically elicited by the activation of a certain neuron group. Our own observations do not, however, show the location of these neurons.

I am glad to know of cases similar to ours, as cited by Dr. Fremont-Smith. His remark that the attack may, perhaps, be associated with a forgotten episode is interesting because our patient during some of the seizures was reminded of her first attack, which was associated with a feeling of sadness.

Concerning Dr. Rosett's question: There must have been a misunderstanding. As Dr. Rosner read the paper, I noticed a sentence toward the end which sounded as though we meant to state that feeling tone response and muscular contractions occurred simultaneously in our patient during her seizures. This did not happen. We were thinking of the physiologic and pathologic processes in epilepsy, which can attack neurons either of feeling tone or of the neuromuscular system.

The remark that seizures were elicited by the hearing of sad music over the radio is interesting. That type of attack opens another field entirely, which lack of time prevents our discussing now. Some leads of interest may be found in that phenomenon.

PATHOLOGIC LAUGHING AND CRYING: A NEUROANATOMIC, NEUROPHYSIOLOGIC AND PSYCHOLOGIC STUDY. DR. CHARLES DAVISON and (by invitation) DR. HAROLD KELMAN.

The occurrence of affective responses, such as involuntary laughing or crying, associated with lesions of the nervous system has been the topic of several contributions. By pathologic laughing and crying we mean involuntary and uncontrollable attacks of emotional expressions as a result of an organic cerebral lesion or lesions. The few attempts at correlation of these emotional expressions on a neuroanatomic and physiologic basis in man have led to various interpretations. The problem is beset by many difficulties, because in most instances the lesions are neither isolated nor limited to specific areas of the nervous system. This is especially true in the case of cerebrovascular disease and multiple sclerosis with multiple and bilateral lesions, in which conditions of pathologic laughing and crying commonly occur. At times, however, these affective responses appear in cases of cerebrovascular disease at the same time as or soon after the ictus. In such cases, with utilization of the other clinical symptoms, a reconstruction of the localization of the lesion responsible for these emotional manifestations may be of value. It is well to remember that the generalized atherosclerotic condition of the cerebral vessels, even in case of single hemiplegias, may cause widespread disturbance in emotional expression.

In order to evaluate properly the part played by the centers and pathways involved, it was found advisable to group cases of this sort, as far as possible, in accordance with the reconstruction of the clinical picture, the onset of the pathologic laughing and crying and the location of the significant lesion. As was demonstrated, these affective responses are present with lesions at various levels of the nervous system, from the cortex to the medulla oblongata. Apparently there are pathways which originate in the cortex and are in intimate connection

with the thalamus, hypothalamus, basal ganglia, mesencephalon and facio-respiratory nuclei. A lesion in any of these centers or along the course of the associated pathways may account for the appearance of such responses. The difficulty of this problem lies in the inability at present to produce experimental lesions in the human being similar to those in animals. These emotions in man are more complex than in animals, and the comparable experimental results in the latter cannot always be applied with accuracy to man.

Our purpose in this contribution was to demonstrate that certain centers and pathways mediate the normal emotional expressions and feelings associated with laughing and crying. When one or several of these centers or pathways are interfered with, deviation from the normal takes place. The response of emotional expression or feeling or its absence, which is considered pathologic, is the effect of the integration of a residual mechanism for these emotional feelings and expressions. The changes induced in the integration of this mechanism may be caused by either destructive or irritative lesions.

In addition to a neurophysiologic interpretation, an attempt, whenever possible, was made to link these disorders with psychologic phenomena. The spasmodic outbursts of laughing or crying associated with the neuroses and psychoses cannot be completely explained on the basis here set forth. Although these will have to be explained on psychologic grounds, their origin and their transmission probably depend on the centers and pathways to be described. In some of the cases included in this paper slight psychotic phenomena in the nature of orientation and memory defects were shown. Although these defects were present, it was always possible to establish sufficient contact with the patients and to determine, by questioning them, that the laughing and crying were spontaneous and uncontrollable and were not stimulated by their own conscious thoughts or environmental situations.

In 33 of 53 cases in which this emotional disturbance was studied clinically autopsy was performed. In 26 cases there was vascular disease of the central nervous system. In the rest the following disorders were presented: tumors, in 6 cases; multiple sclerosis, in 6; amyotrophic lateral sclerosis, in 5, and various neurologic disorders, in 10. Only representative cases from each group were described in detail.

The cases indicated in the following tabulation are described as far as possible in accordance with the location of the lesion.

Level of Lesion	No. of Cases
Cortical	6
Corticodiencephalic	25
Diencephalic	15
Mesencephalometencephalic	7
Total	53

The various psychologic theories for the emotions are discussed. It is emphasized that the pathways and centers mentioned, particularly those of the facio-respiratory mechanism, are most important for the expression of the emotions and that the stimuli setting them off may be cortical or subcortical or both. No single structure is all important, and all must be integrated for control of feeling and expression.

A psychodynamic study of pathologic laughing and crying indicates that a number of variations may occur. These emotions apparently may be adequate or exaggerated in their form or feeling tone, as described by the patient. The responses may also be actually or seemingly disjointed and inappropriate. The spontaneous laughing and crying associated with the psychoses or neuroses are not included in this presentation. Although these responses will have to be explained on purely psychologic grounds, the seat of their origin and their transmission probably depend on the centers and pathways described.

DISCUSSION

DR. HENRY ALSOP RILEY: I have had a rather complete opportunity of hearing Dr. Davison's and Dr. Kelman's exposition of their views. I heard this paper

first as a thesis submitted in partial fulfilment of the requirements for a Doctor of Medical Science. I then heard it at the annual meeting of the American Neurological Association in May 1938, where I had the opportunity of saying a few words with Dr. Kennedy concerning it; I now hear it again. I can recommend no better course of seasoning than this for the preparation of any paper, and I think that the evolution through which this paper has progressed has been of benefit and has crystallized the exposition of the thesis on which it rests. I find myself in almost complete agreement with the authors, and I believe that the views expressed tonight have admirably stated the case in a clear and succinct manner—a difficult thing to do in connection with such an abstruse problem. I do not feel in particular disagreement with any of the views already expressed in regard to the mechanism of these complex behavioral disturbances. That they are such I think no one can deny. They are certainly characteristic only of animals in the phyletic scale which have a cortex. I think there is no question that the animals with which one is currently familiar have no true counterpart of laughing and crying. The evidence which one finds in animals, that which is given principally as an indication of emotional response, is concerned with fear and anger. Beyond that one has practically no knowledge of what might be called the emotional life of an animal. Animals have just as efficient a neuraxis as man. Their hypothalamus is probably as good, if not better, than that of man; their thalamic levels are just as efficient, and their automatic associated movements as complex, as those of man. The great difference between man and animals appears with the development of the suprasegmental organ, the cortex. Certainly, the reactions of laughing and crying are total reactions. Laughing and crying may be elicited by almost any kind of stimulus—whether it is pleasant or unpleasant, whether it is the result of visual, auditory, kinesthetic, visceral or other types of stimuli. The responses may be reversed also in normal persons, who may laugh so heartily that they cry. It is the generally accepted belief that these manifestations are based on activities which take place at the diencephalic level or above it, the corticodiencephalic level or perhaps corticohypothalamic levels.

All are familiar with cases of disease of the spinal cord, the mesencephalic structures, and the basal ganglia, in the vast majority of which, if the lesion is relatively pure and uncomplicated, there are none of the forced laughing and crying reactions. It is only when one reaches the realm of the diencephalon and its connections with the cortex that one is confronted with these complex behavioral disturbances.

I find myself at variance with Dr. Davison when he cites cases in which amyotrophic lateral sclerosis or similar disturbances are a cause of uncontrolled outbursts of disharmonious laughing and crying. All have seen hundreds of such cases, and it is only rarely that one finds these particular emotional disturbances. I believe that when they are present some other factor has entered the situation. Therefore, conclusions as to the localizations of complex behavioral disturbances should not be based on these instances of discrete disease at segmental levels. I believe that something must be added to that picture to result in these unusual phenomena.

The authors of the paper have emphasized the fact, as Dr. Kennedy mentioned last May in his discussion of the paper, that in practically all these cases the clinical histories and pathologic specimens provide evidences of bilateral involvement; it is also of particular significance that in over half the cases which have been used in the preparation of the paper there was arterial disease. When one tries to establish fixed limits to the effect of vascular disease, to pick out particular organs and structures of the nervous system which are affected and to eliminate others which apparently do not show evidence of disturbance, one is on dangerous ground. I believe that disturbances may take place for which later no demonstrable anatomic or histologic cause can be observed. These alterations in function may be physiologic and psychologic, a disturbance in function and not in demonstrable structure. In the case of these disturbances resulting from

arteriosclerosis, in which the lesions seem to be limited to the lower structures, it is impossible and unwise to predicate that they must be explained on the basis only of lesions which can be demonstrated, because there are many lesions producing results physiologically and psychologically which have no anatomic or histologic substratum.

I have benefited materially by this résumé of the subject. The authors have produced interesting corollaries and convincing evidence of the fact that these emotional disturbances depend on a multiplicity of lesions, and on lesions affecting the diencephalic-cortical level. I should be unwilling to accept their proof that these reactions can be produced by lesions below this level. There must be pathways which produce these emotional expressions; otherwise, they could not exist. I cannot believe that a lesion at a level below the diencephalic region can alone produce these complex behavioral reactions. It is my opinion that in the cases in which the lesion seems to be pure it is not pure and that there must be other lesions, perhaps undemonstrable by histologic methods, which are responsible for the manifestations which characterize the syndrome.

DR. NOLAN D. C. LEWIS: Dr. Riley has already mentioned two points that I had intended to emphasize, first, that laughing and crying are not emotions in themselves but are special expressions of certain aspects of fear, anger or sexual feeling, and that laughing and crying are not seen in animals in the evolutionary scale below man. Although animals have various ways of expressing their emotions, which include types of muscular behavior, tail wagging and grimacing, laughter and crying are obviously limited to the action systems of the human being. Although some animal lovers interpret the behavior of their pets at times as representing laughing and crying and some field naturalists have also expressed themselves to that effect, most scientific, unbiased observers disagree with such reports. Both the physical act of laughing and the characteristic mental organization underlying its release are not known for animals as far as any objective evidence is concerned.

Expressions of fear are about as characteristic in animals as in man, but not laughter. This is a more recent development in the field of evolution and has been acquired with the growth of language.

The second point mentioned by Dr. Riley is that the lesions which produce laughing and crying are widespread and it is difficult to make localizations and to find a common denominator. It seems that any serious break between the suprasegmental and the segmental neural mechanisms will produce in some instances the phenomena of pathologic laughing and crying.

Another point which I believe is exceedingly important is the fact that only a certain number of persons with similar lesions show laughing and crying. Müller found that 40 per cent of his group of patients with multiple sclerosis showed laughing and crying and that the others did not give this response. Throughout the field of neuropathology one finds similar differences in response in persons with the same types of lesions. For example, with respect to the simple senile psychoses, I doubt if a neuropathologist can determine by examination of a senile brain whether or not the patient had a senile psychosis. He would certainly be able to say that the brain tissue was senile and to give a detailed description of its appearance, but obviously other factors in the formation of a psychosis enter the picture. I emphasize in this connection that one should seize every opportunity to examine the personality of persons with lesions of the brain. If careful studies of personalities were made one might find interesting indications that would lead to the understanding of differences in reactions. The phenomenon of laughing is produced by amusing situations, by difficult and annoying situations and also by such activities as tickling the ribs, various persons showing differences in their response. In other words, many stimuli will produce the laughing reactions, but these responses have one thing in common: Laughing brings relief of some kind. It seems that in these cases of pathologic laughing and crying there is a drainage for anxiety or tension, which takes place more readily because of a disorder in the neural mechanisms in the deep emotional centers. Why does

one not observe this type of emotional drainage or response with all lesions of the brain? Certainly there is, through the lesion, a severe threat to the main ego organ of the body, the brain, which is the chief integrating structure of the organism. Such lesions constitute a severe threat to the life and functions of the person. Perhaps experience with the neuroses may constitute a bridge to at least partial understanding of the situation in cases of organic disorders.

In some neuroses, particularly in hysteria and in certain obsessional neuroses, as well as in the dreams of normal people, one observes expressions of laughing and weeping which, as is known from investigations, serve as a drainage to relieve anxiety. It seems possible that persons who show spontaneous laughing and crying in association with a lesion of the brain which interferes with integration of the neural mechanisms may be those who are prepared by anxiety or neurotic situations in their life adjustments, and that the accidents and diseases of the brain serve as a release for the expressions, while in most persons who are better integrated or less neurotic a similar lesion of the brain will not produce these symptoms.

I should like to see, whenever possible, thorough personality studies made on persons showing spontaneous laughing and crying, particularly those who have recovered. It would be interesting to know what their earlier personality adjustments have been and whether they have suffered more extensively than the average from neurotic tension.

DR. FOSTER KENNEDY: Does Dr. Lewis mean to be absolute in saying that animals do not laugh? I think that statement is unsound. If one has sufficient experience with dogs one knows they laugh. Darwin's data in "The Expression of Emotion in Animals" are powerful support of one's own observation.

DR. I. S. WECHSLER: I do not want to say anything to cast the slightest aspersion on this paper. I know the work, which represents an enormous amount of thought and effort, but I wonder whether the title is not somewhat erroneous. What Dr. Davison and Dr. Kelman spoke of was neither true laughing nor true crying. They spoke of the pathologic changes in the pathways mediating the motor expression of laughing and crying. One can hardly speak of the pathologic basis of laughing and crying in relation to lesions of the pons or medulla. Laughing and crying are essentially human phenomena. What one sees in animals is an imitation of both, and what one observes in pathologic states is a parody of the one and a travesty of the other. Humor is the highest expression of intelligence. For myself, if I want an almost infallible index of intelligence, I ask whether a man has a deep and genuine sense of humor. I think it is better than any intelligence test that has yet been devised. If, in addition, he also has tact I feel that he is a highly intelligent person. To think of pathologic laughing and crying in the sense of mere departures from normal and to divorce them from their intellectual and emotional contents is, it seems to me, to do violence to concepts. The release is into dissociated, uncontrolled motor bouts of a low level of integration, which are not laughing and are not crying. The mere fact that a person can laugh when he feels sad or cry at a joyous stimulus shows that he has no intellectual or emotional apperception of what is going on in him. An infant of 4 weeks can "laugh" in such a way that it will give the impression it has laughed, and it can also cry early at nothing at all. Infants laugh at things which six months later they will be frightened of, and they cry at funny faces. It is much later when they really begin to laugh and to cry. One needs a cortex to do either or both. Without being facetious or hypercritical, I wonder whether Drs. Davison and Kelman would accept the suggestion as to the change in title.

DR. SANDOR RADO: In any investigation in which one must deal with psychologic and neurologic facts, one always finds oneself struggling with one and the same basic difficulty of method. Owing to this unsolved methodologic problem, even the best psychologic knowledge is organized in a self sufficient way, with little regard for the urgent task of correlating mental and bodily findings. Dr. Wechsler's remarks reflected this state of affairs. He said that the authors' cases

of pathologic laughing could hardly be called instances of laughing in the psychologic sense of the word. Yet I think they illustrate the psychopathology of laughing. Dr. Riley called them cases of forced laughing. One then must ask: forced on whom? Obviously, on the "personality" of the patient, or, more specifically, on his consciously experienced sovereign self. From the subjective point of view of the patient such laughing is unforeseen, uncontrollable and unexplainable in retrospect. He refuses to recognize it as his laughing; yet he cannot fail to see that it was laughing that had occurred in him. Forced laughing is a foreign event in the regulated process of mental life, for it has escaped the integrative efforts of personality functioning. Thus, it can neither serve the purposes nor produce the effects of ordinary laughing; hence the fact, already mentioned by Dr. Lewis, that forced laughing brings no relief.

The findings of the authors seem to indicate that laughing may invade the integrative range of personality functioning in consequence of various kinds of lesions of the central nervous system. Only from studies such as theirs may one hope to learn about the ways in which neural organization and activity create or, if diseased, hamper integrative personality functioning.

In reverting to the paper of Dr. Brickner and Dr. Rosner, it seems to me that they encountered the very methodologic difficulty I have stressed. In his closing remarks, Dr. Brickner said that they made no attempt at localization. If so, what sort of attempt did they make? In looking at morbid alterations of mood or at mental events of any kind from the neurologic point of view, one can consider them only in terms of neural activity, since there is no neurologic alternative to this position.

Dr. E. D. Friedman: May I break a lance for the authors of the paper and illustrate with a case of my own the chief point which Dr. Davison and Dr. Kelman wanted to make, namely, that these phenomena of pathologic laughing and crying are release phenomena? My colleagues and I had an opportunity to observe a patient in the neurologic service of Bellevue Hospital, who was studied clinically for a long time and in whom postmortem examination showed almost symmetric softening of the lower portions of both motor areas, low down. The patient presented as complete a bulbar paralysis as we have seen: the tongue lay limp in the floor of the mouth; she was unable to swallow or show her teeth, but she was subject to bursts of impulsive laughter, so that the ward was in a constant uproar. During these spells, emotional or mimetic innervation of the facial muscles functioned excessively. This case demonstrates almost in experimental fashion the dissociation between voluntary innervation of the facial muscles and the involuntary innervation which is supplied by way of the so-called faciorespiratory pathway of Wilson. In this case the voluntary pathway was seriously damaged on both sides and therefore released the involuntary pathway, with resulting gales of laughter.

Dr. Charles Davison: I wish to emphasize what Dr. Riley has said, that only after a long and careful study did we arrive at our present conclusions. I also wish to thank Dr. Fremont-Smith for the valuable criticism that he has made in reading this paper. We attempted to eliminate, as much as our material permitted, all the loopholes possible, but tonight I find that there are still questions left.

Part of Dr. Riley's criticism is justifiable because many of our patients had cerebrovascular disease and multiple lesions. This, however, was the material we had. To produce experimental lesions in the human subject similar to those in animals is impossible. In a sense we were limited by the experiments produced by nature. These emotions in man are more complex than in animals, and the comparable experimental results in the latter cannot always be applied with accuracy to man. Dr. Riley objects to our attempt to link specific areas of the brain with these emotions. I believe it is justifiable to reconstruct the localization of the lesion responsible for these emotional disturbances by utilizing the associated neurologic findings which have occurred soon after the ictus. If this is not acceptable, one may discard all neurophysiologic concepts, especially the localization of function, for many are based on a correlation of the lesion with the clinical

picture. I agree, however, with Dr. Riley, and this was stressed in our paper, that there is not one particular part of the central nervous system that has to do with laughing and crying. There are various centers and pathways that have to do with these emotions, but at times a lesion in a particular region may set off these emotions. When this occurs, there is justification in stating that the particular area is responsible for the release of laughing and crying.

We have had a few cases of amyotrophic lateral sclerosis. These were studied carefully histopathologically, and in some we observed no evidence of lesions other than those typical of amyotrophic lateral sclerosis, that is, lesions in the motor cortex, pyramidal tracts and anterior horn cells. In other cases the lesion started in the pons or below, and the motor cortex and pyramidal tracts above the pons were free from pathologic changes. Furthermore, in nearly half of a series of about 30 cases of amyotrophic lateral sclerosis I was not able to demonstrate lesions above the pons.

Dr. Wechsler does not believe that lesions below the cortex or diencephalon can produce this phenomenon. I wish to cite our cases in which there were lesions in the mesencephalon and brain stem and Spiller's case in which changes in the affective responses were caused by compression of the pons from an extracerebellar tumor. Furthermore, Magoun and his associates succeeded in producing coordinated facial and vocal activity in response to unilateral and bilateral electrical stimulation of localized areas in the midbrain or pons. This indicates that this kind of phenomenon can take place at lower levels and that pathologic laughing and crying are not necessarily intellectual functions. Infants and mental defectives, as well as very primitive races, indulge, I believe, sufficiently in laughing and crying. Humor, I agree with Dr. Wechsler, is a higher intellectual function, but laughing and crying are not necessarily so. The psychologic aspects we touched on were not those with reference to normal laughing and crying. In normal laughing and crying the adequate stimuli for their elicitation are there—not so in most cases of the pathologic type. We limited ourselves to the aspects of laughing and crying observed in our patients. The pathways and centers concerned with the release of pathologic laughing and crying are the same as those that control normal laughing and crying. The psychologic aspects of normal laughing and crying can stand thorough investigation. In our paper we were not concerned with this.

DR. HENRY ALSOP RILEY: I wish to ask one question. Among the cases in which necropsy studies were made, there was only 1 of amyotrophic lateral sclerosis, was there not?

DR. CHARLES DAVISON: There were others.

DR. HENRY ALSOP RILEY: How many other cases of amyotrophic lateral sclerosis have you seen in which pathologic laughing and crying were shown?

DR. CHARLES DAVISON: There were 5 cases.

DR. HENRY ALSOP RILEY: To my knowledge, I have seen perhaps 10 patients with amyotrophic lateral sclerosis a year, but I have never observed pathologic laughing and crying in any of them. I wish to ask the authors whether, if a series of sections in such a case were mixed with sections in several other cases of amyotrophic lateral sclerosis, they could pick out those in the first case.

DR. CHARLES DAVISON: No, I could not.

BIOCHEMICAL CHANGES ASSOCIATED WITH ALCOHOLIC DELIRIUM. DRS. HERMAN I. WORTIS (by invitation), S. BERNARD WORTIS, PAULA FRANK (by invitation), NORMAN H. JOLLIFFE (by invitation) and KARL M. BOWMAN.

Except for the fact that delirium tremens occurs in cases of habitually severe and chronic alcoholic addiction and that it frequently follows injuries, operations and acute infections, little is known of the etiologic factors that are at play. Since this syndrome was accurately described as long ago as 1813, it is remarkable that no real attempt has been made to study the physiologic and chemical changes which accompany the condition.

Our work at the Bellevue Hospital was initiated by the empiric observations of Keiser and one of us (K. M. B.), who showed that patients with alcoholic delirium did better if they were fed sodium chloride and orange juice and if fluids were forced rather than restricted. The study undertaken was an elaborate one, and I shall present only our positive and pertinent findings.

1. There is evidence of nutritional deficiency in cases of delirium tremens, based on: (*a*) an invariable history of inadequate diet; (*b*) a low vitamin C content of the blood and spinal fluid; (*c*) peripheral neuritis (vitamin B_1 deficiency) in 30 per cent of cases, and (*d*) decrease of serum protein to below normal, according to studies made in Boston.

2. It is now well established that the brain has a respiratory quotient of 1—indicating that for its proper functioning it utilizes sugar. That carbohydrate metabolism is disturbed in cases of delirium tremens is suggested by the following evidence: (*a*) Himwich's work on alcoholism in dogs, showing a lowered oxygen uptake and a respiratory quotient of from 0.8 to 0.9; (*b*) increased lactic acid in the blood and spinal fluid, and (*c*) liver dysfunction in all cases of delirium tremens, resulting in a (1) change in carbohydrate metabolism and (2) decreased activity of the liver as a detoxifying agent, the alcohol thereby being allowed to act longer on the body.

3. The patients are obviously dehydrated. Previous therapy of delirium tremens has been based on the fact that autopsy frequently revealed cerebral edema; therapy was therefore directed at dehydrating the patients. This ignored the obvious dehydration and manifest toxicity of all patients with delirium tremens. Furthermore, our chemical studies revealed that: (*a*) blood chlorides are low; (*b*) chlorides are always excreted as sodium chloride, and (*c*) sodium in being excreted always carries large amounts of water with it.

In summary, it may be said that we have established the following facts:

1. The nutritional factor is important in the production of delirium tremens.

2. The brain is dependent on carbohydrates for its normal functioning, and carbohydrate metabolism and cerebral functioning are both markedly upset in cases of delirium tremens.

3. Persons with delirium tremens are dehydrated; even if cerebral edema exists, it is shortsighted to ignore the dehydration and toxicity of these patients. Fluids should therefore be forced, not withheld.

4. Therapy directed at correcting these metabolic defects has succeeded in reducing the mortality rate for our patients from 16 to 4 per cent.

DISCUSSION

DR. FOSTER KENNEDY: Dr. Wortis, in the presentation, and the other authors, in their work, have given so concise a picture that there is no criticism. I think criticism may be made of the sloppy intellectual attitude that the medical profession had toward this disease before a study of this kind, involving carefully detailed chemical work, was carried out. As long as I have been here, the attitude in New York toward the treatment of delirium tremens has been dominated by one word, "wet brain," showing that man lives not only by bread alone but also by catchwords. This word represented for us the pathology of delirium tremens; no one looked beyond it; on it, apparently, there has been founded a therapy with a large economic notoriety on upper Park Avenue. There, lumbar puncture is carried out on alcoholic patients every day over a period of six months, the idea being that fluctuating pressures of the spinal fluid indicate the alcoholic urge. I am not sure that this absurd system of diagnosis and therapeusis —not a system, but an affectation—is more lamentable than that of others who try to do honest work, without thought. There has been given here a logical, well demonstrated, well investigated procedure of altogether new character for the treatment of a known disease. It should be followed through, for I believe that this is based on a truth and that the old dogma was not a truth.

Book Reviews

Meningiomas: Their Classification, Regional Behavior, Life History, and Surgical End Results. By Harvey Cushing, with the collaboration of Louise Eisenhardt. Price, $15. Pp. 785. Baltimore: Charles C. Thomas, Publisher, 1938.

The emotions and flights of imagination which the honor of receiving the first edition, fresh from the press, of the magnum opus of a Paré or a Hunter might rouse in the breast of a humble reviewer would be food for abstract conjecture. Such an honor has come to this one in the form of Harvey Cushing's new book on the meningiomas. Compiled with patient care and consummate art, in a fragmentary way at first and concentratedly in the last five years, it is truly a stupendous record, nowhere equaled in the world.

The thoughtless reader in his approach to this masterpiece would do well to ponder some of the historical facts. Among them are these: When Cushing had his first opportunity, in 1908, to attack an intracranial meningioma, surgery of the brain was a crude side line of general surgery, with virtually none of the essential present day specialized technic. The operative mortality of tumors of the brain was 50 per cent for explorations alone, to say nothing of attempted removals, so that the surgeon unlucky enough to have this kind of case approached it with a groan and an almost certain presentiment of defeat. The standard of the world today is set by the methods developed almost entirely by Cushing during the subsequent interval of just thirty years, and the mortality at the present time, when radical removal of almost every conceivable tumor is attempted, is lower than 10 per cent.

Neurologic diagnostic methods have been so stimulated that, to use this series of meningiomas as an illustration, Cushing had 1 case during each of the years 1908 and 1909, despite the fact that he was already internationally known and was nearly the sole representative in the field, whereas within twenty years, when there were many competing clinics, he was operating on upward of 30 meningiomas per year, with other varieties of tumor in proportion.

The fact that neurologic surgeons now restrict themselves to this field alone and in addition have become adept neurologists, opthalmologists and roentgenologists, so that they are no longer mere mechanicians, is largely due to Cushing's influence.

The Cushing system of keeping records is generally recognized to be the finest in existence and has been so throughout the years—even those in which "the Chief's" inexorable conscience forced him to do the photography, illustration and other technical chores himself rather than let them go undone. As a result, one finds him able to produce such manifestations of this thoroughness as that on a page containing portraits of the patient in virtually every case described in that particular chapter, no matter how early.

The follow-up of cases in the Cushing Clinic has been so perfected that in this series of 313 all but 2 have been accounted for.

When one reflects that all the advances described and many others are either direct accomplishments of, or chiefly due to, the life and work of Harvey Cushing, his full stature as one of the great surgeons of all time begins to take form.

This book, then, which, more than any of his many works, tells the story of his struggle through the years, depicts in detail the life history of 313 patients who harbored the most surgically dangerous but clinically gratifying lesion known to brain surgery—the meningioma. Ably abetted by Dr. Eisenhardt and drawing

on this vast experience, he reaches conclusions which are necessarily authoritative. The tale and the manner of its telling do not lend themselves to the usual pat remarks concerning style, illustration, format and typographic excellence—though all these are superlative. One must only advise that the book itself be properly held in the hands of each worshiper of the ideal union of the science and the art of writing and of medicine. It is a record of a transcendent natural endowment of extraordinary fortitude, dogged persistence and extreme physical facility, combined with equal intellectual keenness and intuition, and, finally, of that extra spiritual genius which singles out the occasional man to lift him above the ordinary human beings of his day.

Yodoventriculografia (Fosa posterior). By R. Carillo. Paper. Pp. 663, with illustrations. Buenos Aires: El Ateneo, 1937.

"No conscientious surgeon should operate on the posterior fossa without first performing iodoventriculography." The use of iodized oil as a contrast medium in encephalography was introduced by Balado in 1928. Since, the procedure has been utilized in his clinic in approximately 600 cases. The method has been almost universally condemned without trial by non-Argentine authors.

This excellent monograph is devoted to a review of the 100 cases of infratentorial tumor in which an anatomic certification of the lesion was possible. The illustrations leave no doubt of the diagnostic possibilities of the method. The third ventricle, infundibulum, suprapineal recess, aqueduct and fourth ventricle are as sharply outlined as by a metal cast when filling is complete. Incomplete filling is rather common, however. The deformities produced by tumors and obstructions of various types are usually interpretable even without stereoscopy. The method appears to be a real aid to the visualization of tumors of the third ventricle and posterior fossa.

The question of the safety of the method is, of course, paramount. The author states: "Of this enormous number of patients (600) there was not one of whom one could say that the course was aggravated by intolerance of or secondary reaction to the injection of iodized oil. . . . [There has not been] a single death which could be attributed to the iodized oil; it is better tolerated than ventriculography with air. In 100 cases my associates and I were able to study the anatomic specimen. . . . Neither macroscopically nor microscopically did we observe lesions definitely attributable to the iodized oil."

Photomicrographs of the plexuses and ependyma in contact with the oil are shown, and certainly give little evidence of irritation. Slight leukocytosis and increase in protein are found in the fluid; the patients usually have slight fever the day after the injection. Serial roentgenograms show that the oil has left the fourth ventricle by the end of three days. Ordinarily, 5 or 6 cc. is injected. The author appears reasonable in remarking that the distant possibility of harm from the presence of this amount in the lumbar sac is outweighed by the immediate necessity of diagnosis of a dangerous lesion.

The method described appears worthy of trial in other clinics, and it should be obvious that Carrillo's monograph ought to be carefully studied first.

Klinische Untersuchungen an Hirntumoren zur Frage der Entstehung der Stauungspapille. By Georg Anastasopoulos. Price, 23.50 Swiss francs. Pp. 115. Basel, Switzerland: S. Karger, 1937.

This monograph is a study of the relation between the ophthalmologic condition of the optic nerve and tumor of the brain, by the use of clinical examples. The author delineates the various factors which enter into changes in the optic nerve produced by tumors of the brain.